Individual differences in personality associated with anterior cingulate cortex function: Implication for understanding depression

by

Akina Umemoto
B.Sc., University of Oregon, 2007
M.Sc., University of Oregon, 2010

A Dissertation Submitted in Partial Fulfillment
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Supervisory Committee

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Abstract

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We humans depend heavily on cognitive control to make decision and execute goal-directed behaviors, without which our behavior would be overpowered by automatic, stimulus-driven responses. In my dissertation, I focus on a brain region most implicated in this crucial process: the anterior cingulate cortex (ACC). The importance of this region is highlighted by lesion studies demonstrating diminished self-initiated behavior, or apathy, following ACC damage, the most severe form of which results in the near complete absence of speech production and willed actions in the presence of intact motor ability. Despite decades of research, however, its precise function is still highly debated, due particularly to ACC's observed involvement in multiple aspects of cognition. In my dissertation I examine ACC function according to recent developments in reinforcement learning theory that posit a key role for ACC in motivating extended behavior. According to this theory, ACC is responsible for learning task values and motivating effortful control over extended behaviors based on those learned task values. The aim of my dissertation is two-fold: 1) to improve understanding of ACC function, and 2) to elucidate the contribution of ACC to depression, as revealed by individual differences in several personality traits related to motivation and reward sensitivity in a population of healthy college students. It was hypothesized that these different personality traits express, to greater or lesser degrees across individuals, ACC function, and that their abnormal expression (in particular, atypically low motivation and reward sensitivity) constitute hallmark characteristics of depression.

First, this dissertation reveals that reward positivity (RewP), a key electrophysiological signature of reward processing that is believed to index the impact of reinforcement learning signals carried by the midbrain dopamine system on to ACC, is sensitive to individual differences in reward valuation, being larger for those high in reward sensitivity and smaller for those high in depression scores. Second, consistent with a previous suggestion that people high in depression or depression scores have difficulty using reward information to motivate behavior, I find these individuals to exhibit relatively poor prolonged task performance despite an apparently greater investment of cognitive control, and a reduced willingness to expend effort to obtain probable rewards, a behavior that was stable with time on task. In contrast, individuals characterized by high persistence, which is indicative of good ACC function, exhibited high self-reported task engagement and increasing effortful behaviors with time on task, particularly for trials in which reward receipt was unlikely, suggesting increased motivational control. In sum, this dissertation emphasizes the importance of understanding the basic function of ACC as assessed by individual differences in personality, which is then used to understand the impact of its dysfunction in relation to mental illnesses.

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Acknowledgments

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Dedication

To my family, for their endless support and bottomless humor

General Introduction

Everyday cognitive function involves a seemingly infinite number of intact abilities – like paying attention, remembering past and future events, planning, inhibiting impulsive behaviors, learning, exerting effort, socializing, and appreciating rewards – all made possible by complex patterns of activation across the entire brain. Among brain regions the cingulate cortex, a large elongated area on the medial surface of the brain above the corpus callosum that has been described – tongue in cheek – as "the alpha and omega, responsible for all of humankind's functions" (p.12, Gage, Parikh, & Marzullo, 2008), has drawn singular interest from scientists. My dissertation focuses on the function of the anterior portion of it, or anterior cingulate cortex (ACC), known specifically as a key neural substrate of cognitive control. Despite decades of research, however, its precise function is still debated, due particularly to its observed involvement in multiple aspects of cognition. In my dissertation I examine ACC function according to recent developments in reinforcement learning theory that posit a key role for ACC in motivating extended behavior. I hope to understand better the unique and critical role of this brain area in supporting goal-directed behaviors as ACC dysfunction is often implicated in psychiatric disorders such as depression. Accordingly, across four experiments I examined individual differences in personality traits related to motivation and reward sensitivity in order to elucidate the contribution of ACC to mental disorders such as depression. But first, here I present a brief overview of: 1) existing theories of ACC function, 2) a specific theory of ACC function related to reinforcement learning, 3) the midbrain dopamine system, which is believed to carry neural signals for reinforcement learning, 4) electrophysiological signatures of ACC activation, 5) ACC, mental disorders, and the current classification system, 6) ACC and mental disorders as expressed through personality traits, 7) depression and associated dysfunction in cognitive control and reward processing, 8) different aspects of reward processing that may relate to ACC function and to depression, and finally, 9) my aims for the projects presented in this dissertation.

Anterior Cingulate Cortex

Ever since James Papez (1937) included this brain area in his “Papez circuit”, ACC has been known as a part of the limbic system that contributes strongly to emotion processing. ACC is extensively interconnected to prominent limbic regions such as the amygdala, orbitofrontal cortex, as well as autonomic brain stem motor nuclei (Devinsky, Morrell, & Vogt, 1995; Vogt, Sikes, & Vogt, 1993). These connections allow for a variety of neurocognitive processes involving learning and regulation of affect and emotional state. However, recent advances have uncovered a critical role for ACC beyond affective processing that relate more to action generation, cognitive control, and nocioception (Devinsky et al., 1995; Vogt, Finch, & Olson, 1992). In support of these observations, electrical stimulation of ACC has been seen to induce a number of behavioral changes including increased heart rate, changes to affect (mood), involuntary vocalization, speech arrest, and automatic behaviors (see Devinsky et al., 1995 for review; Parvizi, Rangarajan, Shirer, Desai, & Greicius, 2013). One of the unique cytoarchitectural features of ACC is its large layer V pyramidal neurons with extensive dendritic arborizations (Vogt et al., 1993). These neurons project to motor systems including supplementary motor cortex, premotor cortex, the basal ganglia, and the spinal cord (Dum & Strick, 1993; Van Hoesen et al., 1993). Substantial neurophysiological evidence points to ACC’s involvement in motor control (e.g., action generation and execution) or in cognitive processes related to movements (see Devinsky et al., 1995). Striking evidence is demonstrated by a severe form of apathy known as akinetic mutism, which is observed following bilateral lesions of ACC and surrounding areas, and is characterized by the near complete absence of speech production and willed actions in the presence of intact motor ability (Damasio & Van Hoesen, 1983; Devinsky, et al., 1995; Nemeth et al., 1988).

Given the diverse cortical and subcortical input to ACC, ACC has long been considered a key neural substrate where information related to emotion and motivation is translated into voluntary motor activity (Morecraft & Van Hoesen, 1998). A common theoretical framework for describing ACC function subdivides it into an “affective” region in rostral ACC (rACC) and a “cognitive” region in caudal and dorsal ACC (dACC) (Bush, Luu, & Posner, 2000). However, a recent meta-analysis suggests that a region in the caudal and dorsal ACC, termed “anterior midcingulate” cortex, is activated by affective, cognitive and nocioceptive information (Figure 1; Shackman, Salomons, Slagter, Fox, Winter, & Davidson, 2011), and that this region integrates contextually relevant information to shape goal-directed behaviors (Devinsky et al., 1995; Paus, 2001; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004; Rushworth, Buckley, Behrens, Walton, & Bannerman, 2007). Interestingly, this particular area of ACC is a common locus for cingulotomies performed to treat psychiatric disorders, especially obsessive-compulsive disorder (OCD) and depression (Richter, Davis, Hamani, Hutchison, Dostrovsky, & Lozano, 2004).

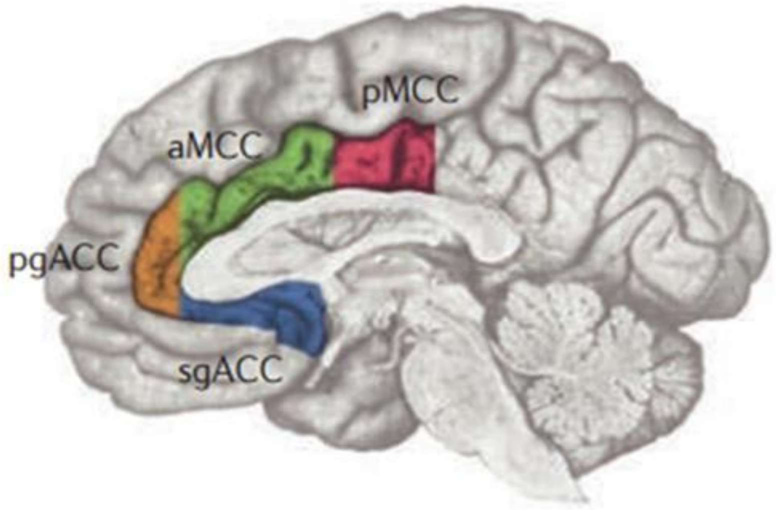

Figure 1. Major subdivisions within the cingulate cortex. A region in the caudal and dorsal subdivision of anterior cingulate cortex (ACC), termed anterior midcingulate cortex (aMCC) in the figure (shown in green), is referred to as the dorsal ACC (dACC) in my thesis. A region rostral to the corpus callosum, termed pregenual ACC (pgACC) in the figure (shown in orange), is referred to as the rostral ACC (rACC) in my thesis. Adapted from Shackman et al. (2011).

ACC, cognitive control, and current theories

A central role for ACC in mediating goal-directed behaviors is well-documented. Particularly, ACC is often co-activated with lateral prefrontal cortex (PFC) and parietal cortex in the service of carrying out “executive” or “cognitive control” functions that tackle a diverse range of cognitive problems (e.g., Corbetta & Shulman, 2002; Fassbender et al., 2006; Sauseng, Klimesch, Schabus, & Dopperlmayr, 2005). These neurocognitive processes facilitate execution of non-automatic or effortful behaviors, particularly in the face of response conflicts or in novel environments (Norman & Shallice, 1986). For instance, if you needed to purchase gasoline when driving home from work one day, cognitive control would be exerted in order to ensure that you take a right-turn into the gas station instead of taking a more familiar left-turn toward home. Although decades of research have elucidated the mechanisms underlying cognitive control (Cohen, Dunbar, & McClelland, 1990; Miller & Cohen, 2001), the exact role that ACC plays in this process is still highly debated. The most prominent theories about ACC function concern performance or conflict monitoring (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Carter, Braver, Barch, Botvinivk, Noll, & Cohen, 1998; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004) and reinforcement learning (Holroyd & Coles, 2002; Rushwoth, Behrens, Rudebeck, & Walton, 2007) (For a more thorough review on the existing theories, see Holroyd & Yeung, 2011). Performance monitoring theories suggests a role for ACC in ongoing behavioral evaluation such that when response conflicts – defined by simultaneous activation of competing responses – or errors occur, cognitive control is applied by ACC in order to recruit dorsolateral PFC (DLPFC), which in turn applies “top-down” biasing signals that overcome conflicts and improve subsequent task performance. Neuroimaging evidence accord with this account, revealing trial-by-trial adjustments in control signals between ACC and DLPFC as a function of response conflicts (Kerns, 2006; Kerns, Cohen, MacDonald, Cho, Stenger, & Carter, 2004). Reinforcement learning (RL) theory of ACC also suggests a role for ACC in instigating trial-to-trial changes in behavior by utilizing RL signals carried by the midbrain dopamine (DA) system (see below), in order to link actions with outcomes for the adaptive modification of behavior (Holroyd & Coles, 2002; see also Sutton & Barto, 1998).

These theories have received support from a vast amount of research, but an important challenge pertains to the consequences of ACC damage. That is, ACC damage typically spares flexible trial-to-trial behavioral modifications based on conflicts (Nachev, 2011; Yeung, 2013) and reinforcement (Kennerly, Walton, Behrens, Buckley, & Rushworth, 2006), observations that are inconsistent with theories of ACC function based on conflict or simple RL processes (Holroyd & Yeung, 2012). The challenge arises partly because the existing theories tend to focus narrowly on specific aspects of ACC function that have failed to account for the hallmark deficits following ACC damage: relatively global impairments to task performance such as response slowing and increased variability in responses (Stuss, et al., 2005; Williams, Bush, Rauch, Cosgrove, & Eskandar, 2004), difficulty integrating reward history over time (Amiez, Joseph, & Procyk, 2006; Kennerly et al., 2006), reduced motivation (Devinsky et al., 1995), decreased production of effortful behaviors (Croxson, Walton, O'Reilly, Behrens, & Rushworth, 2009; Mulert, Menzinger, Leicht, Pogarell, & Hegerl, 2005; Walton, Kennerley, Bannerman, Phillips, & Rushworth, 2006), and in extreme cases with widespread ACC lesions, diminished spontaneous speech and “willed” behaviors as seen in akinetic mutism (Stuss, et al., 2005). Therefore, the field is in serious need for improved understanding of ACC function.

Hierarchical reinforcement learning theory of ACC

Holroyd and colleagues (Holroyd & McClure, 2015; Holroyd & Yeung, 2012) pointed out that recent advances in RL theory based on the framework of hierarchical reinforcement learning (HRL) (Botvinick, Niv, & Barto, 2009; Botvinick, 2012) could provide an answer to this question, proposing a unified theory that explains a number of observations associated with ACC. Specifically, they proposed a critical role for ACC in motivating extended, goal-directed behaviors. Whereas the standard RL approach is concerned with trial-by-trial adjustments in behavior following the delivery of unconditioned reinforcers, HRL develops this approach by representing sequences of primitive, individual actions (e.g., go straight, turn right at the intersection, proceed for two more blocks, etc) as temporally extended behaviors called “options” (or tasks) (such as going to a nearby restaurant) that are selected and reinforced at a higher level of abstraction (Botvinick et al., 2009; Botvinick, 2012). On this view, rather than reinforcing each individual action within a sequence, the entire option can be reinforced and maintained until the option is successfully completed. For example, the ACC would learn that it is better to eat out on a Friday night rather than to cook at home, by way of enforcing an option-specific action policy that maps states of the system (e.g., being hungry) to appropriate actions (e.g., eating out). Although standard RL mechanisms are capable of learning any behavior simply by reinforcing each individual action-outcome association, HRL can afford increased computational efficiency for complex problems characterized by hierarchical structure, which is true of much of human behavior.

Botvinick and colleagues (2009) (Botvinick, 2012) proposed that DLPFC is responsible for option selection and maintenance based on its evident role in applying top-down control over task execution. Alternatively, Holroyd and Yeung (2012) attributed such a role to ACC, proposing that ACC integrates reinforcement history over time to learn the value of options (such as biking in order to stay healthy), and then using this information to select and maintain appropriate options (like biking to work instead of driving) by guiding DLPFC to exert control over the chosen task until the option is terminated (Figure 2). As illustrated in Figure 2, ACC serves as the “conductor” of extended behavior associated with a specific option (e.g., “Get cheese from market”) by learning option values based on the reinforcement signal carried to the ACC by the midbrain DA system (see below), and ensuring that other brain areas (namely the DLPFC and basal ganglia) execute actions that are appropriate to that option. This proposed function of ACC is based on a wide range of observations that have demonstrated involvement of ACC in reward processing, task maintenance and switching, and motivational control over effortful behavior (Holroyd & Yeung, 2012; see also Shenhav, Botvinick, & Cohen, 2013). By this, observations of ACC activation as they relate to the performance monitoring and simple RL functions of ACC can be considered secondary to the core function of ACC, as on this view ACC is not directly involved in the execution of trial-by-trial behaviors. Rather, ACC determines the level of control to apply based on learned task values, and maintains sufficient control in order to ensure that the execution of the option-specific action policy is successfully completed. This explains why trial-to-trial behavioral adjustments are often spared following ACC damage while inducing more global impairments to task performance (see Holroyd & Yeung, 2012).

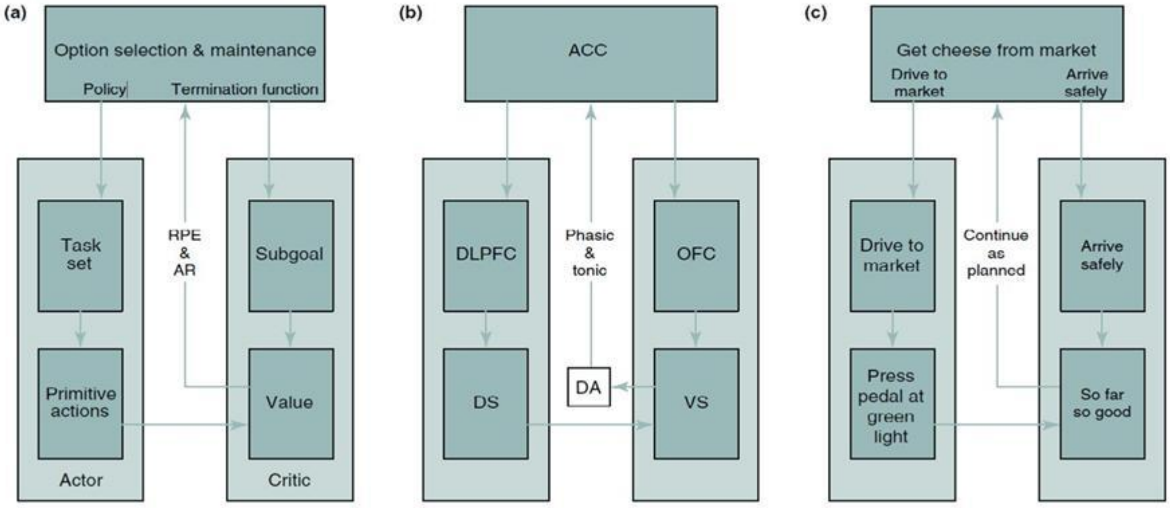

Figure 2. Hierarchical reinforcement learning (HRL) theory as proposed by Holroyd & Yeung (2012) (please see that paper for complete details). (a) Abstract function associated with each component. (b) Proposed neural implementation of the option selection mechanism. (c) An illustrative example of a particular option. ACC sits at the apex of a standard architecture for reinforcement learning to orchestrate high-level option execution: ACC determines the appropriate task to implement given the state of the external environment ("Get cheese from market"). The option-specific action policy ("Drive to market") of the selected task is communicated to DLPFC and basal ganglia (i.e., dorsal striatum, DS), which implements the policy. DLPFC implements the task-set by biasing the activity of DS, which in turn executes individual actions appropriate to the current policy ("Press pedal at green light"). In parallel, ventral striatum (VS) evaluates the progress of DS given the policy. The signal by VS is encoded as a reward prediction error (RPE) signal by the DA system. The RPE signal is then carried to ACC which determines the level of control to apply based on the progress toward the goal state. ACC, anterior cingulate cortex; AR, average reward; DA, midbrain dopamine system; DLPFC, dorsolateral prefrontal cortex; OFC, orbitofrontal cortex. Adapted from Holroyd & Yeung (2012).

Recent computational simulations based on the HRL theory of ACC provide a formal account of ACC's core involvement in task selection and sustaining control over task execution (Holroyd & McClure, 2015). In this model, dACC learns task values by integrating rewards across trials, separately for each option, and switches between options as appropriate (such as choosing to respond to emails or to return phone calls). dACC then ensures that DLPFC and basal ganglia carry out the option-specific motor behaviors (such as picking up a phone, pressing each digit, waiting for the tone, and so on). However, switching between tasks incurs an effortful cost, revealed in behavior as response slowing and increased error rates when individuals switch tasks compared to when they repeat the same task, which are known as switch costs (SCs) (Monsell, 2003). Moreover, the model proposes that the SC penalizes switches between options, such that individuals tend to stay with the same task even if a different task is associated with greater reward value. The theory further suggests that SCs are attenuated by a control signal applied by the rACC, which makes switching between options by dACC easier. By this, rACC is said to implement a “meta-option” (e.g., starting a work day instead of taking a day off) and apply a control signal over dACC, which reduces the SC and facilitates switches between options consistent with the meta-option. The degree of control is regulated according to the overall reward value of the meta-option, which is determined by averaging rewards across options. Thus, if the reward value of a chosen option declines as performance on particular task worsens (seen in increased errors and fewer rewards), then rACC would ramp up control over dACC, facilitating a shift by dACC to a more rewarding option. Conversely, the control signals gradually decrease so long as a high-reward value is maintained (Holroyd & McClure, 2015). This hierarchical formation of ACC function is based on the assumptions that frontal cortex is hierarchically organized along a rostral-caudal midline (see Holroyd & McClure, 2015). Further, the direct anatomical connectivity between rACC and dACC (Jones, Groenewegen, & Witter, 2005) and functional connectivity between them as seen in fMRI likely facilitate the neural communication within ACC (Nakao, et al., 2010). Moreover, a few studies have indicated that rACC is involved in reducing SCs (Wager, Jonides, Smith, & Nichols, 2005; see also Pollmann, Weidner, Müller, & Cramon, 2000).

The midbrain dopamine system

Traditionally considered as the “pleasure center” in the brain, the midbrain DA system was believed to encode a hedonic signal that represents the pleasure associated with reward consumption (Wise, 1980). However, this notion has since been challenged. Striking evidence comes from an influential study by Schultz and colleagues who recorded the activity of midbrain DA neurons in monkeys (Figure 3). The DA neurons initially exhibited a fast, phasic increase in activity in response to the unexpected delivery of reward. However, after the monkeys learned a particular stimulus-reward association, the phasic burst of DA in response to reward delivery was no longer observed, which is inconsistent with the “pleasure center” idea. In turn, the DA neurons responded to the conditioned, reward-predictive stimulus, suggesting that these signals “travel back in time” with learning to the earliest indication of forthcoming reinforcement. Critically, when the expected reward was omitted, the DA neurons instead exhibited a phasic decrease in activity at the time of the reward omission. These observations led the researchers to propose that the DA neurons track the errors in the prediction between the actually obtained reward and expected reward, known as a reward prediction error (RPE) signal, producing phasic increases and decreases in activity when ongoing events are better or worse than expected, respectively (Schultz, Dayan, & Montague, 1997; Bayer & Glimcher, 2005; Niv, 2009; Schultz, 2010). These dynamic signals appear to serve as a “temporal difference error”, which is an important learning signal used in powerful RL algorithms (Sutton & Barto, 1998). The RPE signal is said to be carried to many parts of the brain, prominently to basal ganglia, PFC (including ACC), and amygdala, for the adaptive modification of behavior (Holroyd & Coles, 2002; Montague, Hyman, & Cohen, 2004). In so doing, the signal provides a formal mechanism for instantiating the renowned “Law of Effect”, which states that action probabilities are higher for rewarded actions and lower for punished actions (Thorndike, 1911).

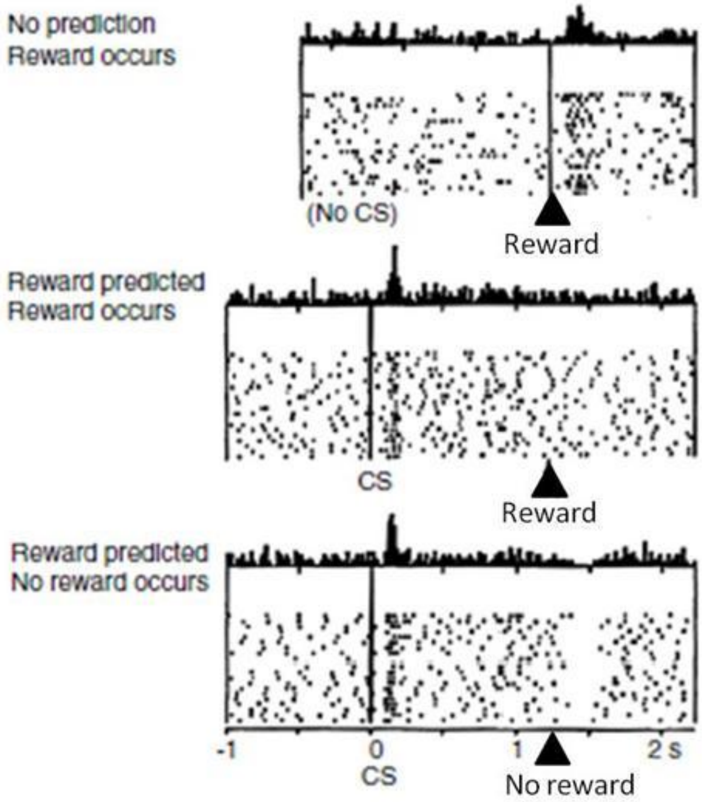

Figure 3. Midbrain dopamine (DA) reward prediction error (RPE) signals. Raster plots depict DA cell activity during individual trials; histograms at the top of each raster plot depict activity pooled across trials. Top: DA neurons initially exhibit phasic increases in activity at the time of reward delivery. Middle: After the stimulus-reward association is learned, the conditioned stimulus (CS) elicit a phasic increase in DA activity (at time 0 second (s)) rather than at the time of expected reward. Bottom: When the predicted reward was not delivered, the DA neurons exhibit phasic decrease in activity at the time of unexpected reward omission. Adapted from Schultz et al. (1997).

Schultz's seminal work has been supported by series of animal studies demonstrating that manipulation of dopaminergic neurons (for example, with DA receptor antagonists) do not change animals' responses to primary rewards (like consumption of sweet water) or subjective ratings of pleasure in humans. Rather, DA system manipulation powerfully changes how much effort rats put into obtaining rewards (like the number of lever presses) (Ikemoto & Panksepp, 1999; Salamone & Correa, 2002; Salamone, Cousins, & Snyder, 1997), and how much human participants desire and approach rewards (Berridge & Kringelbach, 2015; Berridge & Robinson, 1998). Berridge and colleagues elegantly summarized the function of the midbrain DA system such that it does not affect immediate feelings of pleasure (reward "liking"), but rather, it motivates reward-seeking behavior (reward "wanting") by attaching "incentive salience" to reward stimuli (Berridge & Robinson, 2003). Accordingly, the midbrain DA RPE signals carrying incentive salience of stimuli affects behaviors in a way that cause the animal and human subjects to approach rewards more often in the future (Holroyd & Coles, 2002).

Electrophysiological signatures of ACC – Reward Positivity and Frontal Midline Theta

The electroencephalogram (EEG) has provided a valuable tool for measuring ACC activity from electrodes placed on the human scalp. Work by Holroyd and Coles (2002) proposed that the impact of the fast, phasic midbrain DA RPE signals carried to ACC is observable on the human scalp in a component of the human event-related potential (ERP). Referred to as the reward positivity (RewP) (or more commonly known as the feedback error-related negativity or feedback negativity), this component is sensitive to the valence of performance feedback (reward vs. no-reward (or error)) (Miltner, Braun, & Coles, 1997). It is characterized by a phasic decrease in activity approximately 250 ms following an onset of negative (or error) feedback and a phasic increase in activity following the onset of positive (or reward) feedback around the same time (Figure 4a). RewP was originally thought to be sensitive to negative performance feedback (as the name "negativity" indicates), however, a number of more recent studies have indicated that positive feedback mainly drives the valence effect seen in the RewP (hence the name "reward positivity") (Holroyd, Pakzad-Vaezi, & Krigolson, 2008; Proudfit, 2015). Because RewP is commonly measured as a difference wave (i.e., the negative deflection subtracted from the positive deflection) (see Holroyd & Krigolson, 2007), it is known as a negative-going ERP component despite its name. The RewP is defined partly by its scalp distribution, which is maximal over front-central areas of the head (Figure 4b) (Walsh & Anderson, 2012 for review). Moreover, a recent meta-analysis supports the proposal that RewP indexes DA RPE signals (Sambrook & Goslyun, 2015; see also Walsh & Anderson, 2012). Converging evidence suggest dACC as the neural generator of RewP, stemming from source localization studies (Miltner et al., 1997; Gehring & Willoughby, 2002), simultaneous EEG/fMRI recordings (Becker, Nitsch, Miltner, & Straube, 2014), transcranial direct current stimulation (Reinhart & Woodman, 2014), and intracranial recording in monkeys (Emeric, Brown, Leslie, Pouget, Stuphorn, & Schall, 2008) and rodents (Warren, Hyman, Seamans, & Holroyd, 2015). RewP amplitude is also correlated with fMRI BOLD signals in ventral striatum which is a major target of the DA system, indicating a strong DA-RewP link (Carlson, Foti, Mujica-Parodi, Harmon-Jones, & Hajcak, 2011; Foti, Weinberg, Dien, & Hajcak, 2011; Proudfit, 2015).

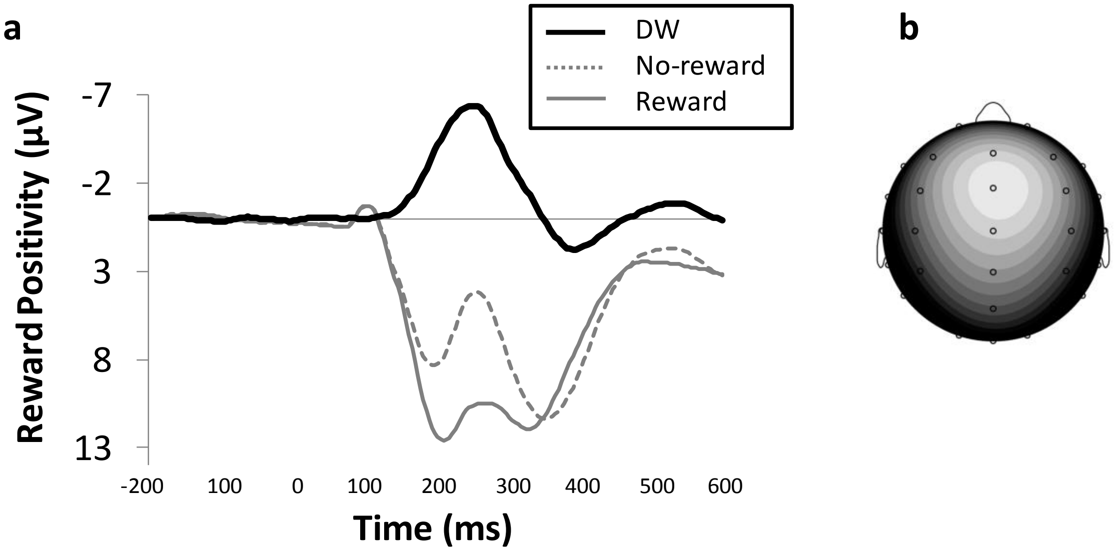

Figure 4. Example grand-average (i.e., averaged across subjects) event-related brain potentials (ERPs) elicited time-locked to the onset of reward feedback (at 0ms). The x-axis indicates time (ms) and the y-axis indicates voltage (μV). (a) Reward positivity (RewP) measured at channel FCz (i.e., over the frontal-central areas of the scalp) as a difference wave (DW: black), calculated by subtracting the reward ERP (gray line) from the no-reward ERP (dashed gray line). Negative is plotted up by convention. (b) Voltage distribution for RewP at the maximum negativity. Data derived from Experiment 2 of this thesis.

Substantial evidence also indicates that neural oscillations in the theta frequency range (approximately 4 to 8 Hz) measured in the EEG recorded at the human scalp, known as frontal midline theta (FMT), reflect ACC activity. Source localization studies point to ACC as the neural generator of FMT (Asada, Fukuda, Tsunoda, Yamaguchi, & Tonoike, 1999; Ishii et al., 1999; Luu & Tucker, 2001; Scheeringa, Bastiaansen, Petersson, Oostenveld, Norris, & Hagoort, 2008), and electrical stimulation of ACC induces FMT (Talairach et al., 1973). FMT has also been associated with a number of high-level cognitive processes including attention, memory, cognitive control, and effort (Ishihara & Yoshii, 1972; Jacobs et al., 2006; Itthipuripat et al., 2013; Rutishauser et al., 2010; Smit, Eling, Hopman, & Coenen, 2005; for review, Cavanagh & Frank, 2014; Hsieh & Ranganath, 2014; Mitchell, McNaughton, Flanagan, & Kirk, 2008). Willed generation of motor behavior (e.g., commission of erroneous responses) and perceptions (e.g., delivery of performance feedback) have been observed to enhance FMT power and induce phase-reset of FMT (see Cavanagh, Zambrano-Vazquez, & Allen, 2012). FMT is believed to enable ACC to orchestrate neural processes related to goal-directed behaviors including the execution of effortful behaviors (see Holroyd 2013, 2016). Moreover, low frequency oscillations including FMT are thought to provide an ideal mechanism for facilitating neural communication between spatially distal brain areas (Buzsaki & Draguhn, 2004). A number of studies have demonstrated FMT phase synchrony between ACC and other cortical sites including lateral PFC, motor cortex, and sensory cortices (Cavanagh & Frank, 2014, for review), which is broadly consistent with the proposal that ACC orchestrate higher-level options (Holroyd & Yeung, 2012; Holroyd & McClure, 2015). Moreover, FMT power rises with time on task as mental fatigue increases (Boksem, Meijman, & Lorist, 2006; Lorist, Klein, Nieuwenhuis, De Jong, Mulder, & Meijman, 2000), particularly for demanding, effortful tasks such as the Stroop task and arithmetic calculations (Barwick, Arnett, & Slobounov, 2012; Kamzanova, Metthews, Kustubayeva, & Jakupov, 2011; Kiroy, Warsawskaya, & Voynov, 1996; Wascher et al., 2014). Current thinking relates mental fatigue -- which is associated with declines in cognitive performance including attention, working memory, and cognitive control (Boksem et al., 2006; Lorist et al., 2000) -- to reduced motivation to continue on a given mental task. For instance, motivational incentives could partially counteract the adverse effect of mental fatigue on performance (Boksem et al., 2006; Lorist, Benzdan, ten Caat, Span, Roerdink, & Maurits, 2009; Tops & Boksem, 2010). Likewise, evidence suggests that the midbrain DA system underlies the effect of mental fatigue on task performance (Boksem et al., 2006; Lorist, Boksem, & Ridderinkhof, 2005; Lorist & Tops, 2003).

ACC, mental disorders, and the current classification system

Why is ACC function so essential to understand? As one might expect given the high-level cognitive processes associated with ACC, its dysfunction has been often reported in a number of psychiatric disorders, including schizophrenia, substance abuse, attention-deficit hyperactivity disorder (ADHD), OCD, and depression. Most current systems for diagnosing mental disorders are based on subjective reports of behavioral symptoms, as commonly determined using manuals like the Diagnostic and Statistical Manual of Mental Disorders (DSM) by American Psychiatric Association (APA) and the International Statistical Classification of Diseases and Related Health Problems (ICD) by the World Health Organization (WHO). These manuals classify mental disorders categorically based on the number of symptoms individuals report. Although they have provided psychologists and psychiatrists an essential common language by standardizing diagnostic criteria, this classification approach has also raised a number of important challenges. First, the classification is dichotomous: a person is determined to either have or not have a disorder. For instance, if an individual has one symptom short of the required number of symptoms for, say, depression, he will be classified as “non-depressed”. This raises a second challenge related to the profiles of individuals with mental disorders. As these manuals require individuals to exhibit only a certain number of symptoms out of a set of possible symptoms (e.g., “yes” to 5 out of 9 symptoms), two individuals with the same disorder can exhibit a totally different symptom profile as it is possible to have only one or two symptoms overlapping between them (e.g., one person with depression could have insomnia and weight loss, while another person with depression might oversleep and show weight gain). And third, and importantly, such categorical classification methods complicate diagnosis due to high co-occurrence among mental disorders (for example, depression often co-occurs with anxiety or substance abuse). These challenges further highlight a lack of consistency in the underlying neuro-cognitive impairments in each mental disorder. For instance, comorbid disorders can diminish the response typically observed in the primary disorder (Gorka, Huggins, Fitzgerald, Nelson, Phan, & Shankman, 2014; Kentgen, Tenke, Pine, Fong, Klein, & Bruder, 2000; Weinberg, Klein, & Hajcak, 2012). Clearly, a re-evaluation of this classification approach is needed not only to better understand the nature of mental disorders, but also to improve their diagnosis and treatment.

Supporting this, the United States National Institute of Mental Health has recently introduced a new research framework to understand mental disorders. Known as the Research Domain Criteria (RDoC) framework, the approach no longer classifies mental disorders categorically based on self-reported symptoms, but rather provides insight into the causal factors underlying the disorders based on empirical findings (Insel et al., 2010). Specifically, the RDoC framework motivates the identification of basic functional dimensions that underlie human behavior (e.g., impulsivity), which are understood to vary across individuals in terms of their degree of expression, from normal to abnormal (e.g., from not at all impulsive to extremely impulsive), and which can be analyzed at multiple levels of analyses (i.e., genes, molecules, cells, circuits, physiology, neuroimaging behavior, self-reports, and task paradigms). This initiative currently includes five high level “domains” of functions that reflect five major systems related to emotion, cognition, motivation, and social behavior: Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Systems for Social Processes, and Arousal and Regulatory Systems. Further, each of these domains are said to contain specified “constructs” (or concepts) representing a basic functional dimension of behaviors, which are analyzed using various technique as described above. For instance, the “Positive Valence Systems” domain includes the following five constructs: “approach motivation”, “initial responsiveness to reward attainment”, “sustained responsiveness to reward attainment”, “reward learning”, and “habit”. Each construct can be further broken into “subconstructs”. For instance, the construct “approach motivation” is composed of the subconstructs “reward valuation”, “willingness to work”, “reward prediction error”, and “action selection”, each of which is subject to further analysis.

The RDoC approach avoids the problems of categorical and dichotomous classification as each individual's behavior falls somewhere within a spectrum of possible behaviors. Moreover, co-morbidity no longer becomes a problem as it may point to the same underlying mechanism (e.g., impaired reward valuation underlying both depression and addiction). I believe that this framework can be readily utilized to understand why so many psychiatric disorders are associated with ACC dysfunction. Striking support for this is that ACC is indicated in all five major domains of functions described above. As I will relate below, particular dimensions of personality appear to be associated with ACC function, which when expressed to an extreme degree can contribute to a number of psychiatric disorders.

ACC, personality, and mental disorders

The HRL theory of ACC (Holroyd & Yeung, 2012; Holroyd & McClure, 2015) makes specific predictions about the contribution of ACC to behavior, namely, that ACC motivates the selection and maintenance of extended, goal-directed behavior based on learned task values. Critically, from the RDoC perspective, the theory suggests that particular personality traits should relate to ACC function. On this view, dysfunction of ACC should impair effortful control over extended, goal-directed behavior and reward processing. This dovetails with the behavioral changes observed following ACC damage as reviewed earlier. In fact, accumulated evidence from behavioral (Gusnard et al., 2003), neuroimaging (Kurniawan, Seymour, Talmi, Yoshida, Chater, & Dolan, 2010), and electrical stimulation (Parvisi, et al., 2013) studies in humans and single-unit recordings in monkeys (Blanchard, Strait, & Hayden, 2015) suggests that ACC is associated with persistence (and the lack thereof as occurs in apathy (Levy & Dubois, 2006; Robert, et al., 2009; van Reekum, Stuss, & Ostander, 2005)) and reward sensitivity (Bress & Hajcak, 2013; Keedwell, Andrew, Williams, Brammer, & Phillips, 2005; Liu, Wang, Shang, Shen, Li, Cheung, & Chan, 2014; Pizzagalli, 2011). Tellingly, abnormal levels of these traits appear to link ACC with mental disorders. For instance, a number of studies have revealed deficits in effortful control in depression (Cohen, Lohr, Paul, & Boland, 2001; Hartlage, Alloy, Vazquez, & Dykman, 1993; Zakzanis, Leach, & Kaplan, 1998).

Likewise, depression, particularly when associated with high levels of anhedonia, is associated with reduced propensity to work for reward (Clery-Melin, Schmidt, Lafargue, Baup, Fossati, & Pessiglione, 2011; Treadway, Bossaller, Shelton, & Zald, 2012; Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009; Treadway & Zald, 2011), decreased reward feedback processing in EEG (Liu et al., 2014), and reduced ACC activity as observed in fMRI studies (Harvey, Armony, Malla, & Lepage, 2010; Mies, Van den Berg, Franken, Smits, Van der Molen, & Van der Veen, 2013; Steele, Kumar, & Ebmeier, 2007; Wacker, Dillon, & Pizzagalli, 2009).

Other disorders associated with ACC corroborate these observations. In our laboratory, we have observed that a motivational deficit commonly seen in children with ADHD was associated with reduced RewP, which is normalized by acquisition of relatively salient monetary incentives as compared to abstract performance feedback (Umemoto, Lukie, Kerns, Müller, & Holroyd, 2014). RewP is likewise reduced for monetary reward feedback in substance-dependent individuals, but its amplitude is comparable to that of controls following receipt of salient drug reward (i.e., cigarette puffs) (Baker, Wood, & Holroyd, in press). Furthermore, the negative symptoms of schizophrenia have been attributed to an impaired ability to associate actions with reward values (Gold, Waltz, Prentice, Morris, & Heerey, 2008; Morris, Holroyd, Mann-Wrobel, & Gold, 2011; Morris, Quail, Griffiths, Green, & Balleine, 2015), resulting in reduced effortful behaviors (Barch, Treadway, & Schoen, 2014; Gold, Kool, Botvinick, Hubzin, August, & Waltz, 2014; Gold, Strauss, Waltz, Robinson, Brown, & Frank, 2013). Finally, a smaller RewP has been observed in people with Parkinson’s disease who are apathetic, but not in control subjects or people with Parkinson’s disease who are non-apathetic (Martínez-Horta et al., 2014). More tellingly, the dACC of healthy individuals high in apathy was significantly less activated for actions that demanded higher effort levels (Bonnelle, Manohar, Behrens, & Husain, 2015).

Focusing on depression and its underlying neuro-cognitive dysfunction

In my dissertation I utilize the HRL-ACC theory to investigate, in a population of healthy college students, how individual differences in personality related to ACC function contribute to one of the most common mental disorders worldwide: depression. Depression is defined as a period of at least two weeks during which there is either depressed mood most of the day, nearly every day, or loss of interest or pleasure (i.e., anhedonia) in most activities for most of the day (i.e., DSM; APA, 2013). In addition to these two core symptoms, DSM requires at least four other symptoms that reflect changes in behavior relative to a person's regular functioning: changes in weight/appetite, sleep (insomnia or hypersomnia), activity (psychomotor agitation/retardation), fatigue or loss of energy, guilt/worthlessness, difficulty concentrating, and suicidality. Depression holds "ignominious status as a world leader in disease burden" (Greden, 2001, p. 30), imposing a significant public health problem and financial burden and impairing the affected individuals socially, occupationally, and individually (WHO, 2012). In Canada, 11.3% of adults on a community survey reported having symptoms that met the criteria for depression at some point during their lifetime (Pearson, Janz, & Ali, 2013), with the depression occurrence generally higher for women than men (APA, 2013). Although many treatments are available (e.g., pharmacological, cognitive therapy, etc), low complete recovery and high relapse rates associated with depression impose a significant challenge to its treatment (Gaynes et al., 2009; Trivedi & Daly, 2008). In addition to antidepressants taking time to enact changes in the brain, probability for positive treatment responses to antidepressant medication (Trivedi et al., 2006) and to psychotherapy (DeRubeis et al., 2005) does not exceed 50%. Furthermore, it has been consistently reported that the first episode of major depression is a strong predictor of the second episode (i.e., more than 50%), which in turn predicts future episodes with even higher rates (Kessler & Wang, 2009). Even if remission is achieved, relapse rate in the next 2 years reaches 40% or higher (Boland & Keller, 2009). Moreover, depression is the major cause of suicide (Rihmer, 2001). These facts indicate a strong need for prevention, early diagnosis, and effective treatment.

Despite decades of research using a variety of methodological techniques in humans and animals, the pathophysiology and etiology of depression are still not fully understood. A long history of research has demonstrated a variety of cognitive dysfunctions in depression, namely biased information processing toward negative events (Beck, 1976; De Raedt & Koster, 2010; Matt, Vazquez, & Campbell, 1992) and reduced responses to positively-valenced stimuli (for review, Gotlib & Joormann, 2010; Pizzagalli, 2014). Along with a variety of cognitive control impairments, a recent meta-analysis also indicated general motor slowing in depression (Snyder, 2013). Although both the negativity bias and blunted reward responses have been highlighted, reduced reward sensitivity has been consistently reported in laboratory experiments. Particularly, Pizzagalli and colleagues (Pizzagalli, Jahn, and O'Shea, 2005) have developed a task that requires integrating reward history across trials for the purpose of reward-based decision making (e.g., in order to learn that one stimulus is three times more rewarding than another stimulus). Whereas healthy non-depressed individuals show a response bias toward rewarding stimuli (i.e., they are more likely to choose the rewarding stimuli), both non-clinically and clinically depressed individuals fail to develop such a bias (Pizagalli, 2014 for review; Pizzagalli, Losifescu, Hallett, Ratner, & Fava, 2008; Pizagalli et al., 2005). Interestingly, this selective impairment was not due to trial-by-trial responses to reward but rather to impaired integration of reinforcement history over multiple trials. This impairment correlated with anhedonia symptoms, suggesting that deficient reward integration may be at the core of the reward processing deficit associated with anhedonia (Pizzagalli et al., 2008; Vrieze et al., 2013). Moreover, the blunted response to rewards appears to remain after the remission of depression, pointing to a possible vulnerability for relapse (Pechtel, Dutra, Goetz, and Pizzagalli, 2008). Additionally, healthy individuals failed to develop the reward response bias when DA activity was pharmacologically attenuated, indicating involvement of the midbrain DA system in modulating such reward learning (Pizzagalli et al., 2008). Evidence for blunted reward sensitivity was further supported by Kunisato and his team (2012) using a different task that also depended on the participants' ability to integrate both reward and no-reward outcomes.

Compatible evidence has emerged in the EEG literature where a series of careful investigations by Hajcak and colleagues have demonstrated that RewP – which is sensitive to traits related to "reward sensitivity" (Bress & Hajcak, 2013) -- may serve as a potential depression biomarker (Proudfit, 2015). Reduced RewP amplitude has been consistently found both in healthy college students who exhibit high levels of depression symptims and in depressed patients (Bress, Smith, Foti, Klein, & Hajcak, 2012; Foti, Carlson, Sauder, & Proudfit, 2014; Foti & Hajcak, 2009; Liu et al., 2014; but see Mies, van der Veen, Tulen, Birkenhäger, Hengeveld, & van der Molen, 2011 and Tucker, Luu, Frishkoff, Quiring, & Poulsen, 2003), consistent with a fMRI study which reported a smaller RPE signal in dACC (Kumar, Waiter, Ahearn, Milders, Reid, & Steele, 2008). Importantly, internal reliability and test-retest reliability of RewP over the course of two years is high (Bress, Meyer, & Proudfit, 2014; Segalowitz, Santesso, Murphy, Homan, Chantziantoniou, & Khan, 2010). The RewP modulation is also specific to depressive symptoms and not related to anxiety, which is highly co-morbid with depression (Bress, Meyer, & Hajcak, 2015). Strikingly, blunted RewP was already observable in pre-pubertal children aged 8 to 13 (Bress et al., 2012), and predicted the first onset of major depressive episode in adolescent girls by the two year follow-up (Bress, Foti, Kotov, Klein, & Hajcak, 2013).

Some studies have also suggested an association between FMT and anhedonia as it relates to performance feedback processing (Mueller, Panitz, Pizzagalli, Hermann, & Wacker, 2015; Padrão, Mallorquí, Cucurell, Marco-Pallares, & Rodriguez-Fornells, 2013), yet more evidence indicates that FMT power is higher in anxious individuals, presumably due to their heightened sensitivity to uncertain events (Cavanagh & Shackman, 2015, for review). Although whether FMT can serve as a neural marker for depression (or anxiety) remains a question (Gold, Fachner, & Erkkilä, 2013), substantial evidence has demonstrated a strong link between the theta activity in rACC at rest (i.e., when participants are not engaged in a particular cognitive task) and depression (Pizzagallil, 2011 for review). Theta power positively correlates with rACC glucose metabolism (Pizzagalli, Oakes, & Davidson, 2003), and an influential study by Mayberg and colleagues demonstrated that increased resting glucose metabolism in rACC prior to pharmacological treatment predicted better treatment response in patients with depression (Mayberg et al., 1997). Countless studies since then have indicated a robust relation between increased resting theta power in rACC and positive responses to a variety of treatment options (e.g., sleep deprivation, transcranial magnetic stimulation, various drugs) (Pizzagalli, 2011).

Pizzagalli (2011) provided a conceptual framework for understanding depression at an integrative circuit level, with a particular emphasis on hypoactive cognitive control areas in dACC and DLPFC and hyperactive areas in amygdala and the surrounding limbic regions (e.g., subgenual ACC) (Davidson, Pizzagalli, Nitschke, and Putnam, 2002; Mayberg et al., 1997; Pizzagalli, 2011). Hypoactive frontocingulate activation was already apparent in unmedicated adolescents with depression, indicating that this abnormality may appear in the early phase of the disorder (Halari et al., 2009) and may not normalize when symptoms improve (Aizenstein et al., 2009). Pizzagalli (2011) proposed that rACC serves as a key hub within a default mode network (DMN) (e.g., Buckner, Andrews-Hanna, & Schacter, 2008; Raichle, MacLeod, Snyder, Powers, Gusnard, & Shulman, 2001), which is a network of brain areas that is active and functionally connected when individuals are not engaged in any overt cognitive tasks or in goal-directed behaviors (i.e., at rest). The DMN is generally interpreted as reflecting self-referential processes, including introspection, remembering, and planning as related to oneself (Broyd, Demanuele, Debener, Helps, James, & Sonuga-Barke, 2009; Buckner et al., 2008; Raichle et al., 2001). Conversely, when individuals engage in goal-directed behavior, especially for tasks that require cognitive or attentional control, the DMN is deactivated and a task positive network (TPN) involving the dACC and DLPFC comes online (Corbetta & Shukman, 2002; Sounuga-Barke & Castellanos, 2007). A number of studies have supported such dynamic shift between DMN and TPN (Mckiernan, Kaufman, Kucera-Thompson, & Binder, 2003; Pallesen, Brattico, Bailey, Korvenoja, & Gjedde, 2009; Tomasi, Ernst, Caparelli, & Chang, 2006), and reduced deactivation of DMN (i.e., DMN not fully deactivated) has been associated with attentional lapses (Weissman, Roberts, Visscher, & Woldorff, 2006) and errors (Li, Yan, Bergquist, & Sinha, 2007), thereby interfering with task performance. Pizzagalli suggests that impaired suppression of DMN and failure to recruit TPN, together with impaired modulation of amygdala activity by rACC, contributes to an excessive, maladaptive form of self-referential processing known as rumination, which is characterized by a repetitive negative thinking pattern related to oneself (Nolen-Hoeksema, 1991). Rumination predicts depression onset and severity, and prolongs symptom duration (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008, for review), which encourages a vicious cycle involving sustained attention to negative information.

Parsing reward processes and the role of midbrain dopamine system

There is an evident link between depression and ACC on the one hand, and reward sensitivity and reduced motivation for effortful control on the other. Yet, how ACC is involved in these personality traits is still poorly understood. Accumulating evidence suggests that reward processing is not a unitary construct and entails temporal dynamics characterized by a number of distinct processes such as reward learning, valuation, anticipation, acquisition, and integration, which are highly interrelated concepts (Berridge & Kringelbach, 2015; Berridge & Robinson, 1998; 2003; Berridge, Robinson, and Aldridge, 2009). This has a significant implication for understanding anhedonia, a cardinal symptom of depression (Klein, 1974), which has emerged as one of the most promising endophenotypes (i.e., narrowly defined and quantifiable phenotypes with a clear genetic connection) of depression (Berghorst & Pizzagalli, 2010; Hasler, Drevets, Manji, & Charney, 2004). As the term indicates a person with depression has been considered as having difficulty *enjoying* pleasurable events. Yet, evidence for this has been mixed (see Pizzagalli, 2014; Treadway & Zald, 2011). Almost three decades ago Klein (1987) reported that patients with depression have appeared to enjoy rewards that were readily available but complained about feeling no desire to obtain them (e.g., Dichter, Smoski, Kampov-Polevoy, Gallop, & Garbutt, 2010), and suggested two ways by which hedonic capacity can be modulated. Anticipatory hedonia relates to one’s capacity to anticipate and approach reward, underlying motivation and goal-directed behavior (i.e., “wanting”), while consummatory hedonia relates to in-the-moment pleasure or reward response (i.e., “liking”). This differentiation has been increasingly advocated by research in non-human animal (Berridge & Kringelbach, 2015; Berridge & Robinson, 1998; 2003), and in human neuroimaging (Dillon, Holmes, Jahn, Bogdan, Wald, & Pizzagalli, 2007; Knutson, Fong, Adams, Varner, & Hommer, 2001) and electrophysiological (Novak & Foti, 2015; Pornpattananangkul & Nusslock, 2015) studies (also see Waugh & Gotlib, 2008, for behavioral evidence, and Der-Avakian & Markou, 2012, for review).

An endeavour to tease apart discrete reward processes in the depression literature has been growing. As mentioned earlier, consummatory reward processes appear intact in individuals with depression (Pizzagalli, 2014; Sherdell, Waugh, & Gotlib, 2012; Treadway & Zald, 2011). For instance, pleasure ratings of sweet tastes and humorous cartoons were similar between depressed and non-depressed individuals (Dichter et al., 2010; Sherdell et al., 2012), while self-reported anticipatory anhedonia in depression predicted reduced effort to view humorous cartoons (Sherdell et al., 2012). A recent study outside of the laboratory setting corroborated those findings: although depressive symptoms were associated with a decreased response to positive events and lower positive affect, adolescents who exhibited symptoms of depression and anhedonia reported enjoying pleasurable experiences in daily life as much as those low on these symptoms (van Roekel et al., 2015).

To investigate motivational deficits associated with anhedonia, Treadway and colleagues developed a reward-based effortful decision-making paradigm called the Effort-Expenditure for Rewards Task (EEfRT, pronounced “effort”; Treadway et al., 2009) in which participants are asked on each trial to choose between completing a high effort task to receive a larger monetary reward and a low effort task to obtain a smaller reward. They found that individuals high in anhedonia and patients with depression exhibited reduced propensity to expend effort for rewards, especially when the reward stakes were larger (as compared to the reward stakes for the easier task) or more probable (Treadway et al., 2009; Treadway et al., 2012), highlighting impaired effortful behavior in depression (Barch, Treadway, & Schoen, 2014; Treadway et al., 2009; Treadway et al., 2012. But see also Sherdell, Waugh & Gotlib, 2012). Further analysis based on patients’ self-reports revealed that this effort-related deficit was correlated with anhedonia for wanting rather than anhedonia for liking (Treadway et al., 2012). Treadway and colleagues demonstrated that DA activity underlies willingness to exert effort for rewards using the same EEfRT paradigm (Treadway et al., 2012; Wardle, Treadway, Mayo, Zald, & de Wit, 2011), consistent with evidence in the animal models that DA modulates effort-based decision-making (Salamone, Correa, Farrar, & Mingote, 2007, Salamone, Correa, Farrar, Nunes, & Pardo, 2009).

Summary and Aim

More than a decade of research has attributed the role of ACC to cognitive control processes and decision-making, most notably as it relates to the trial-by-trial adjustment in behavior based on response conflicts and reinforcement (Botvinick et al., 2001; Holroyd & Coles, 2002). The success of these theories notwithstanding, a key challenge remains as to why such transient behavioral modifications are often preserved following ACC damage, which indicates that the computational and functional specificity of ACC in mediating these processes remains unclear. Holroyd & Yeung (2012) pointed out that the impact of ACC damage on task performance is relatively global in nature – response slowing and variability, inability to sustain rewarded behaviors across multiple trials, and reduced motivation to produce effortful behaviors – and proposed a theory of ACC function according to principles of HRL. Based on accumulating evidence that support ACC's involvement in task selection and maintenance, reinforcement learning, and effort-based decision making, the HRL-ACC theory proposes that ACC is responsible for motivating effortful control over extended, goal-directed behaviors. Specifically, ACC learns higher-level task (option) values based on the reward signals (i.e., RPE signals) carried to the ACC by the midbrain DA neurons, and using those learned task values motivates the selection and maintenance of a task until it is completed. Therefore, one can imagine that ACC damage should lead to difficulty in learning task values in order to motivate and sustain extended behaviors -- such that the individual might stay home in bed rather than going out with friends or working on a project.

Critical to my dissertation, ACC dysfunction is implicated in a number of psychiatric disorders, a focus of which in my dissertation is depression. A multitude of observations now suggest deficits in reward processing and motivation of effortful behavior underlying this common, persistent, and recurrent mental disorder, supporting the ACC-depression link. Moreover, an electrophysiological signature of ACC, RewP, has been proposed to potentially serve as a depression biomarker. Likewise, FMT in ACC at rest has drawn attention in the medical and clinical fields as a promising predictor for treatment response to antidepressant medication. However, a number of questions arise: what are these neuro-electrophysiological markers really telling us about normal and abnormal function of ACC? The aim of my dissertation is to elucidate this question based on the recent HRL-ACC theory and in terms of the RDoC framework, which conceptualizes disorders as dimensional behaviors that every individual exhibits, with varying degrees from normal to abnormal (e.g., he is more impulsive, she is more reserved). Specifically, the HRL-ACC theory predicts that particular personality traits should relate to ACC function. In the series of four experiments, I investigated individual differences in personality associated with ACC function, mainly reward sensitivity and motivation, and their implication for understanding depression symptoms. Individual differences in personality were measured among healthy college students by administering multiple personality questionnaires. The specific aim of each experiment is described below. Experiments 1 to 3 are electrophysiological investigations while Experiment 4 is a purely behavioral investigation.

Specific Aims and Four Experiments

Experiment1: Growing evidence suggests that impaired reward processing underlies depression, but a better understanding of exactly what aspect of reward processing is impaired is needed. A number of studies have indicated that depression in both the non-clinical and clinical populations is associated with reduced RewP amplitude. However, it is important to examine the blunted RewP in relation to other reward processes, particularly processes related to reward anticipation, as increasing evidence suggests a link between anhedonia and impaired anticipatory process (or reward "wanting"). Moreover, given that depression has been associated with impaired reward integration, especially when reward delivery is intermittent, one can ask: How does reduced RewP amplitude interact with reward learning in depression? Hence, I examined how individual differences in personality related to ACC function were associated with reward learning, anticipation, and outcome processing in Experiment 1. For this, participants were presented with one of five cues on each trial and had to learn response-reward associations by trial and error while their brainwaves were recorded. I then analyzed several reward processing ERP components in relation to individual differences in personality.

Experiment 2: What appears least explored in the cognitive control literature is the maintenance of task performance. The HRL-ACC theory proposes a key role for ACC in maintaining extended behavior. But in the depression literature, sustained behavior has received little interest. One study suggested that patients with depression have difficulty sustaining positive emotion (but not negative emotion) over time as indicated by reduced fronto-striatal bran activation (Heller et al., 2009). In Experiment 2 I investigated the role of ACC in sustaining task performance for a prolonged period of time and examined how particular personality traits were related to extended task performance. For this purpose I employed a standard time estimation task commonly used to elicit RewP. Participants were asked to estimate 1 second on each trial while their brainwaves were recorded, and performed this simple task continuously (with short breaks between blocks) for 2 hours to obtain reward. The RewP and FMT were examined in relation to several personality traits that I propose are related to ACC function.

Experiment 3: Experiment 3 extended Experiment 2 by investigating sustained task performance and decision-making involving physical effort, as opposed to cognitive effort, as non-human animal studies have revealed ACC involvement in physically demanding tasks and voluntary task selection. Recent studies suggest that high depression scores are associated with reduced willingness to expend effort to obtain rewards, and I extended this finding by having participants engage in an effortful task for 1 hour. Participants used a hand-dynamometer and were asked to choose between carrying out an easy choice (i.e., squeezing the dynamometer with relatively less force) and hard choice (i.e., squeezing with relatively more force) to obtain smaller or larger rewards, respectively, while their brainwaves were recorded. Task choice over time was examined in relation to personality traits, RewP amplitude, and FMT.

Experiment 4: This experiment focused on the aspect of ACC function involved in task selection, as opposed to task maintenance. Particularly, the HRL-ACC theory makes specific predictions about how the rostral and caudal/dorsal sectors of ACC apply control in a hierarchical manner (Holroyd & McClure, 2015). On this view, the dACC learns the values of tasks and selects tasks based on those learned values (by averaging the value of rewards received during task execution), and the rACC learns the value of the meta-option (i.e., superordinate task) by averaging the value of rewards received during its execution (i.e., across tasks). Further, whereas the dACC applies a control signal that sustains performance on the selected task, the rACC applies a control signal that facilitates switches by dACC between tasks (which dACC is not always able to accomplish on its own due to an effortful cost associated with task switching). We employed a voluntary task switching paradigm in which participants were free to choose for themselves which one of two tasks to perform on each trial, thereby allowing an investigation of an interplay between cognitive control and task selection. Furthermore, as the theory predicts that particular personality traits should be associated with ACC function, several personality questionnaires were administered to investigate the relation between traits related to motivation and reward sensitivity as well as rumination (as it relates to rACC function) and task switching performance.

Dealing with outliers

In this dissertation I utilized multiple linear regression analyses for all four experiments in order to examine how individual personality questionnaire scores predicted task performance and neural activity. However, these correlation-based analyses are highly sensitive to the presence of outliers. To account for the potential influence of outliers, I utilized the following jackknife approach. For each dependent variable, the same multiple regression analysis was performed multiple times by a method of leave-one-out (i.e., by excluding the data for a different participant at each iteration) (Hewig et al., 2011). Based on the result of each iteration, if any single participant was found to contribute uniquely to the final regression model—in that removing their data resulted in an inclusion or exclusion of one or more personality predictors from the model, and the same result was not obtained by the other iterations within the same analysis – then the data of this participant were excluded from the given analysis. For each iteration the criterion for including or excluding particular personality traits was based on a minimum p-value of 0.1 (see also “Data Analysis” in Experiment 1). This procedure was applied to each multiple regression analysis conducted in each experiment. The degrees of freedom indicate the number of participants included in each analysis. I chose this method of dealing with outliers over other methods (such as excluding participants who exceeded a criterion threshold based on particular number of standard deviations) because this jackknife approach 1) was not confounded by experimenter bias, as it provided an objective method for removing outliers systematically across analyses, and 2) ensured that the reported results were robust against, and less sensitive to the contribution of any individual participant.

The jackknife method excluded between zero to four participants across experiments and tests, with 1.5 participants removed on average.

Experiment 1

Numerous studies have observed impaired reward processing in depression, particularly when depression symptoms included anhedonia (see Der-Avakian & Markou, 2011; Pizzagalli, 2011, for review). In particular, many recent experiments have parsed distinct reward-related processes associated with reward anticipation and consumption, partly on the basis of influential work in non-human animals that has revealed physiological differences between these processes (see Berridge et al., 2009; Schultz, 2007). However, the exact nature of impaired reward processing in depression is still not fully understood, as evident in inconsistent experimental results across the literature (e.g., Knutson & Heinz, 2014). Abnormal reward processing associated with reward anticipation and outcome processing have been implicated in the fMRI literature on depression (Knutson, Bhanji, Cooney, Atlas, & Gotlib, 2008; Santesso, Bogdan, Birk, Goetz, Holmes, & Pizzagalli, 2012; Smoski, Felder, Bizzell, Green, Ernst, Lynch, & Dichter, 2009). For instance, hypoactivation of striatal regions (including the nucleus accumbens) has been observed during reward anticipation (Pizzaggali et al., 2009; Smoski et al., 2009; Stoy et al., 2012; but see Gorka, Huggins, Fitzgerald, Nelson, Phan, & Shankman, 2014 and Knutson et al., 2008) and during reward acquisition (Forbes eta l., 2006; Pizzagalli et al., 2009; Smoski et al., 2009). Reduced orbitofrontal cortex (OFC) activation during these processes has been also reported (Forbes et al., 2006; Pizzagalli, 2014; Smoski et al., 2011; see also Schaefer, Putnam, Benca, & Davidson, 2006). Moreover, when individuals with high depression scores or people who exhibit high levels of negative affect anticipate monetary rewards or pleasant images, dACC and/or rACC activity are sometimes enhanced (Knutson et al., 2008; Gorka et al., 2014; see also Dichter et al., 2012) and sometimes reduced (Smoski et al., 2009; Smoski eta l., 2011). By contrast, another study found no group differences in dACC activation during reward anticipation (Pizzagalli et al., 2009). These discrepancies may stem from differences in task design. For instance, a common experimental paradigm in fMRI research assesses reward anticipation using the monetary incentive delay (MID) task, which typically involves a speeded response following the end of an anticipation period (Knutson, Bhanji, Cooney, Atlas, Gotlib, 2008). By contrast, other studies of reward processing require behavioral responses prior to the beginning of an anticipation period (Smoski et al., 2009), or involve purely passive tasks (Gorka et al., 2014). As well, studies utilizing the MID task have examined reward anticipation in relation to neural activity elicited by predictive cues (e.g., Knutson et al., 2008), while other studies have examined this process in relation to neural activity during the delay period prior to reward delivery (Gorka et al., 2014; Smoski et al., 2009). Furthermore, subject groups have varied greatly across the different studies in terms of their demographics and other individual differences, especially regarding medication status and the presence or absence of comorbid disorders (such as anxiety).

In the EEG literature, reward anticipation has been studied by examining differences in hemispheric processing in the EEG recorded over frontal cortex, which is termed frontal EEG asymmetry (Davidson, 1992; Davidson, 1998). The frontal EEG asymmetry is hypothesized to reflect motivational propensities to engage in approach versus avoidance behavior, such that relatively greater left frontal activity is associated with an increased tendency to approach positively-valenced stimuli, while relatively greater right frontal activity (or reduced left frontal activity) is associated with an increased tendency to avoid negatively-valenced stimuli. Individuals with depression who exhibit negative affect often produce less left frontal activation (Jesulola, Sharpley, Bitsika, Agnew, & Wilson, 2015, for review). A recent study that utilized both EEG and fMRI measures indicated that increased left hemisphere activity relative to right hemisphere activity during reward anticipation in healthy adults reflects increased activation of left dACC and OFC (Gorka, Phan, & Shankman, 2015). More interestingly, recent evidence indicates that individuals with early-onset depression (i.e., onset during childhood or adolescence) -- a subgroup of depressed individuals who have been described as exhibiting an impairment in reward anticipation (Klein, Durbin, & Shankman, 2009) – but not individuals with late-onset depression produce less left frontal activity relative to right frontal activity (Nelson, Shankman, & Proudfit, 2014; Shankman et al., 2007; Shankman et al., 2013). The underlying mechanisms and functional significance of frontal EEG asymmetry are still poorly understood, which may partly explain the inconsistent findings associated with reward anticipation in depression, especially as they relate to ACC.

Despite inconsistent evidence for impaired reward processing in the fMRI literature (e.g., Smoski et al., 2009; Smoski et al., 2011; Steele, Kumar, & Ebmeier, 2007), a growing body of evidence suggests that depression is associated with a reduced RewP -- an electrophysiological signature of the impact of midbrain DA reward signals on ACC in response to reward feedback that has been associated with self-reports of reward sensitivity (see introduction). However, evidence for smaller RewP in depression should be understood in relation to other reward processes. For instance, given that RewP amplitude is modulated by learning-related factors and is sensitive to the probability of reward occurrence, impaired reward learning would be expected to disrupt the amplitude of the RewP. Consistently, depression has been associated with impaired reward learning (Kunisato et al., 2012; but see also Chase, Frank, Michael, Bullmore, Sahakian, & Robbins, 2010), particularly when reward delivery is intermittent (see introduction; Kumar et al., 2008; Pizzagalli et al., 2008), which could stem from reduced reward valuation as indicated by the smaller RewP in depression. Conversely, a blunted RewP could be associated with increased anticipation of reward because RewP amplitude is inversely correlated with reward expectancy (see below, Holroyd et al., 2003; Holroyd & Krigolson, 2007; Holroyd et al., 2009; Sambrook & Goslin, 2015).

In view of recent reports that have emphasized the need to distinguish between these different reward processes as they relate to depression (e.g., Der-Avakian & Markou, 2011), I recorded brainwaves from participants engaged in a reinforcement learning task in order to examine how individual differences in personality traits related to ACC function are associated with different components of reward processing. The ERP technique allows for investigation of continuous, dynamic changes in neural activity, providing temporally precise information regarding distinct reward-related processes (Novak & Foti, 2015; Pornpattananangkul & Nusslock, 2015). On each trial subjects were required to press one of two buttons in response to one of five visual cues, which they determined by a process of trial and error. To delineate the dynamics of reward processing, I examined four ERP components (see also Novak & Foti, 2015; Pornpattananangkul & Nusslock, 2015). First, as a measure of reward sensitivity, outcome processing was examined using the feedback-related RewP. Second, because the dopamine RPE signals propagate back in time with learning from feedback stimuli to events that predict the outcomes (see introduction), I examined the cue-related RewP as a neural indication of reward anticipation in response to reward predictive external stimuli. Third, I examined the readiness potential, a negative-going deflection in the ERP recorded from over motor areas of cortex prior to response execution (Shibasaki & Hallett, 2006). The readiness potential, which has been utilized as a measure of motor response preparation (Kornhuber and Deecke, 1965), is sensitive to motivational influences; for instance, readiness potential amplitude increases (i.e., becomes more negative) with increased levels of participant engagement, or when rewards are provided to participants (Kornhuber & Deecke, 1965; McAdam & Seales, 1969). Fourth, as an index of outcome anticipation, I examined the stimulus preceding negativity (SPN), which is characterized by negative slow waves that precede the occurrence of predictable events, specifically in anticipation of forthcoming feedback stimuli (Brunia, 1988; Brunia & Damen, 1988; Brunia, Hackley, van Boxtel, Kotani, & Ohgami, 2011, for review). SPN is sensitive to motivationally relevant outcomes, increasing in amplitude (i.e., becoming more negative) when participants anticipate forthcoming monetary rewards (Kotani, Kishida, Hiraku, Suda, Ishii, & Aihara, 2003; Ohgami et al., 2006; Fuentemilla, Cucurell, Marco-Pallarés, Guitart-Masip, Morís, & Rodríguez-Fornells, 2013) or positively-valenced stimuli (Böcker, Brunia, & van den Berg-Lenssen, 1994; Böcker, Baas, Kenemans, & Verbaten, 2001; Donkers & van Boxtel, 2005; Howard, Longmore, & Mason, 1992). Note that both cue-RewP and SPN are considered to reflect reward anticipation processes, but the former relates to a relatively transient neural response to reward predictive stimuli, whereas the latter relates to a relatively sustained neural response in anticipation of forthcoming feedback stimuli.

In addition, participants completed several personality inventories that were used to assess individual differences in motivation and reward sensitivity as they relate to ACC function. I then analyzed the relationships between the above ERP components and these personality traits. Because depression is not a unitary construct, this measure was examined from a broader perspective by examining a variety of associated symptoms. It was predicted that traits related to reward sensitivity – i.e., high reward responsiveness, low anhedonia and depression scores – would be associated with feedback-related RewP such that participants high in reward sensitivity would exhibit a large feedback-related

RewP whereas those high in depression scores would exhibit a small feedback-related RewP (Bress & Hajcak, 2013; Liu et al., 2014; Cooper, Duke, Pickering, & Smillie, 2014). It was also predicted that traits related to anticipation of future outcomes – i.e., anticipatory pleasure and intolerance of uncertainty – would be associated with increased and decreased SPN, respectively, according to the degree to which reward delivery was anticipated or desired. Importantly, as depression has been associated with impaired reward anticipation, participants high in depression scores were expected to produce an abnormal SPN, although I had no specific prediction about the direction of this effect (reduced or enhanced). Although the analyses regarding cue-RewP were exploratory, traits associated with outcome anticipation (e.g., anticipatory pleasure and intolerance of uncertainty) were expected to modulate cue-related RewP similarly to their effects on SPN as both components tap into processes related to reward anticipation. I had no specific predictions regarding the readiness potential. Finally, as depression has been associated with impaired reward learning, participants high in depression scores were expected to perform the learning task worse than other subjects.

Materials and methods

Participants

Sixty-eight undergraduate students were recruited from the University of Victoria Department of Psychology subject pool to fulfill a course requirement or earn bonus credits. All subjects (7 males, 9 left-handed, age range=17-26 years, mean age =20 +/- 1.9 years) had normal or corrected-to-normal vision. Each also received a monetary bonus in addition to the credits, the amount of which depended on their task performance (see below). All subjects provided informed consent as approved by the local research ethics committee. The experiment was conducted in accordance with the ethical standards prescribed in the 1964 Declaration of Helsinki.

Task Design

Participants performed a probabilistic reinforcement learning task (Figure 5) in which one of five possible cues (3.5 by 3.5 cm), selected at random, was presented for

800 ms on each trial. These five cues were randomly selected from a set of ten different images from different object categories (Figure 5, bottom). Immediately following cue offset a small white cross (.5 by .5 cm) appeared at the center of the screen, to which participants were instructed to make a response. Participants were told to respond by freely choosing either the “Z” key or the “/” key within a 500 ms response limit, after which the image of the small white central cross was replaced with a blank screen for 1 second, followed by the appearance of a feedback stimulus. If the participant responded within the 500 ms deadline, the 1 second delay was extended by the time remaining between their response and 500 ms deadline (e.g., if the response time was 200 ms, then the remaining 300 ms was added to the 1 second delay, resulting in a total delay of 1300 ms on that trial). If participants failed to respond within 500 ms the message “Respond quickly!” was presented immediately following the deadline and the same trial was repeated. Otherwise, after the delay period, a feedback stimulus (3.5 by 3.5 cm) was presented for 800 ms, consisting of either a white circle or a white diamond representing reward and no-reward, the mappings of which were counterbalanced across participants. Finally, the next trial started after an inter-trial interval (ITI) of 600 ms during which a small black fixation dot was presented at the center of the screen. Unbeknownst to the participants, each of the five cues was uniquely associated with a reward probability of either 100%, 75%, 50%, 25%, or 0% for one of the two possible responses (hereafter called the “correct response”), whereas the other response to each cue (hereafter called the “incorrect response”) always resulted in no-reward feedback. One of the two response keys was chosen randomly to serve as the correct response for two of the four cues associated with the 100%, 75%, 50%, or 25% reward probabilities, while the other response key served as the correct response for the remaining two cues. For the 0% reward probability cue, the “correct” response was chosen randomly between the two response keys, but both correct and incorrect responses for this cue always resulted in no-reward. Halfway through the experiment the five cues were replaced with the remaining 5 cues from the set of ten cues (Figure 5, bottom), requiring participants to learn the appropriate stimulus-response mappings anew.

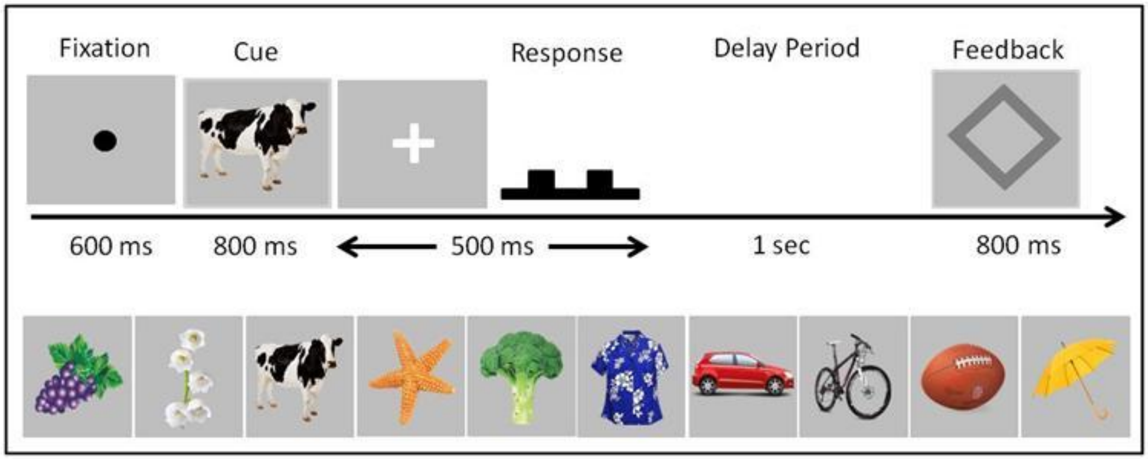

Figure 5. An example sequence of one trial and a set of ten cue images used during Experiment 1.

Questionnaires

Participants completed a total of six personality questionnaires related to motivation, reward sensitivity, and depression symptoms, administered through LimeSurvey on the same computer where the task was performed. First, I used the Persistence Scale (PS: Cloninger, Svrakic, & Przybeck, 1993), which contains 20 items answered on a scale of 1 (definitely false) to 5 (definitely true) that assess the tendency to overcome daily challenges. Second, I used the Ruminative Responses Scale (RRS: Nolen-Hoeksema et al., 1994), which contains 22 items answered on a scale of 1 (almost never) to 4 (almost always) that measure the propensity to ruminate in response to depressed mood. Third, I used the Reward Responsiveness Scale (Van den Berg, Franken, & Muris, 2010), which is a self-report measure of reward-related behavior developed in part on the Behavioral Inhibition/Activation Scale (Carver & White, 1994), to provide a relatively pure measure of reward responsiveness. The Reward Responsiveness Scale contains 8 items answered on a scale of 1 (strong disagreement) to 4 (strong agreement). Fourth, I used the Temporal Experience of Pleasure Scale (TEPS), which contains 18 items answered on a scale of 1 (“very false for me”) to 6 (“very true for me”) that assess two components of hedonic capacity, namely consummatory pleasure (TEPS-C: i.e., “liking” or in-the-moment experience of pleasure) and anticipatory pleasures (TEPS-A: i.e., “wanting”) (Gard, Gard, Kring, & John, 2006). Fifth, I utilized the 12 item, short-form of the Intolerance of Uncertainty Scale (IU), which measures sensitivity to and avoidance of uncertain and ambiguous situations (Carleton, Norton, & Asmundson, 2007; Freeston, Rhéaume, Letarte, Dugas, & Ladouceur, 1994). Items were answered on a scale of 1 (not at all characteristic of me) to 5 (entirely characteristic of me). Sixth, I used the 21 item, short-form of the Depression Anxiety Stress Scale (DASS-21) (Lovibond & Lovibond, 1995) to measure severity of depression, anxiety, and stress, according to a scale that ranged from 0 (“did not apply to me at all”) to 3 (“applied to me very much, or most of the time”). Summed total scores were used for each of the questionnaires such that high scores indicated, respectively, high persistence, high reward responsiveness, high hedonic capacity (or reduced anhedonia), high rumination, high intolerance of uncertainty, and high depression, anxiety, and stress symptoms. In order to minimize the duration of the experiment, the neutral or non-negatively framed questionnaires (the Persistence Scale, the Reward Responsiveness Scale, and TEPS) were administered half-way through the task (i.e., at the end of 8th block) and the questionnaires related to depressive symptoms (RRS, IU, and DASS-21) were administered at the completion of the experiment. The rumination scale and the stress subscale of the DASS-21 were not included in the analyses as they tended to strongly correlate with other variables (for example, anxiety and depression scores) and were also not the primary focus of the study.

Procedure

Participants were seated comfortably in front of a computer monitor (1024 by 1280 pixels) at a distance of about 60 cm in an electromagnetically shielded dimly lit room. The task was programmed in Matlab (MathWorks, Natick, MA, USA) using the Psychophysics Toolbox extension (Brainard, 1997; Pelli, 1997). Subjects rested the fingertips of their index fingers comfortably on two response keys (see below) of the computer keyboard. Participants were provided with both written and verbal instructions that explained the procedure, and were told to maintain correct posture and to minimize head movements and eye blinks during the experiment. They were instructed that they would be presented with one of five cue images on each trial and to respond to each cue by pressing either of two specified response keys (see above), after which they would see a feedback stimulus (Figure 5). They were further instructed to press one of the 2 keys after the cue disappeared and was replaced with a small central white cross. Half of the participants were told that an image of a white circle indicated that they earned a 2 cents reward and an image of a white diamond indicated that they did not earn any reward; the feedback-reward mappings were reversed for the other half of the participants. Participants were informed that they should perform the task as best as they could in order to maximize their reward earnings, and that all of the money that they earned would be theirs to take home at the end of the experiment. In addition, participants were told that some cues were associated with a higher reward probability than the other cues, and that they should respond as quickly as possible.

Participants first performed a practice block consisting of 30 trials. The practice block utilized two cue images randomly selected from a set of 5 images (i.e., a chair, a house, a shoe, a soccer ball, and a frying pan) that were not used in the actual experimental blocks. In the practice block the correct response differed for the two cues (i.e., left response for one cue and right response for the other cue), but was associated with an 80% reward probability for both cues, thus exposing the participants to the probabilistic nature of the task. Participants earned between 10 and 25 cents from the practice block. The practice trials were followed by the task proper, which consisted of 16 blocks of 60 trials each. Each cue appeared 12 times in each block. The experiment consisted of 2 phases, each consisting of 8 blocks. When the 8th block was completed (Phase 1), participants were given a small break during which they answered several demographic questions (related to age, gender, history of concussion, medication status, and so on) and three personality questionnaires (see above) on the computer screen. The second half of the experiment (Phase 2) resumed afterwards; participants were told that they would continue performing the same task with five new cues. When the experiment was completed, participants answered the three remaining personality questionnaires (see above) and were paid their reward earnings, which varied approximately from CAN$5 to $10.

ERP Data Acquisition and Pre-processing

The electroencephalogram (EEG) was recorded using a montage of 41 electrode sites in accordance to the extended international 10–20 system (Jasper, 1958). Signals were acquired using Ag/AgCl ring electrodes mounted in a nylon electrode cap with an abrasive, conductive gel (EASYCAP GmbH, Herrsching-Breitbrunn, Germany). Signals were amplified by low-noise electrode differential amplifiers with a frequency response high cut-off at 50 Hz (90 dB–octave roll off) and digitized at a rate of 250 samples per second. Digitized signals were recorded to disk using Brain Vision Recorder software (Brain Products GmbH, Munich, Germany). Interelectrode impedances were maintained below 20 kΩ. Two electrodes were also placed on the left and right mastoids. The EEG was recorded using the average reference. The electroocculogram (EOG) was recorded for the purpose of artifact correction; horizontal EOG was recorded from the external canthi of both eyes, and vertical EOG was recorded from the suborbit of the right eye and electrode channel Fp2.

Post-processing and data visualization were performed using Brain Vision Analyzer software (Brain Products GmbH). The digitized signals were filtered using a fourth-order digital Butterworth filter with a passband of 0.10–20 Hz. Segmentation of epochs of data differed depending on the type of stimuli analyzed. For the cue and reward feedback processing, an 800 ms epoch of data extending from 200 ms prior to 600 ms following presentation of each stimulus (i.e., cue or feedback) was used to segment data for waveform analysis. For the readiness potential an 1800 ms epoch of data extending from 1400 ms prior to 400 ms following response execution was used. For the SPN, a 3300 ms epoch of data extending from 200 ms prior to 3100 ms following presentation of each cue stimulus was used. Ocular artifacts were corrected using an eye movement correction algorithm (Gratton, Coles, & Donchin, 1983). The EEG data were re-referenced to linked mastoids electrodes. Data were baseline corrected by subtracting from each sample the mean voltage associated with that electrode during the 200 ms interval preceding stimulus onset for all the components, except for the readiness potential which used the 200 ms interval between 1200 ms and 1400 ms preceding response execution. Muscular and other artifacts were removed according to 150 μV Max-Min voltage difference, ±150 μV level threshold, a ±35 μV step threshold, and a 0.1 μV lowest allowed activity level as rejection criteria. ERPs were then created for each electrode and participant by averaging the single-trial EEG according to the reward and no-reward conditions for the feedback stimuli, for each probability condition, separately for the cue, response, and delay periods.

Data Analysis

Following convention the feedback-RewP was measured at channel FCz, where it reaches maximum amplitude (see below), utilizing a difference wave approach that isolated the reward positivity from overlapping ERP components such as the P300 (Holroyd & Krigolson, 2007; Sambrook and Goslin, 2015). Furthermore, feedback-RewP amplitude was evaluated post-learning. For each reward probability cue, participants were considered to have learned the cue-response association when three consecutive correct responses were made (see also Fuentemilla et al., 2013; Morris, Heerey, Gold, & Holroyd, 2008). Feedback-RewP was analyzed in the blocks after this criterion was reached for each reward probability condition. ERPs were then averaged across reward probability as follows (cf. Holroyd & Krigolson, 2007; Holroyd et al., 2009): for each participant the ERP to reward feedback stimuli in the 100% reward probability condition (100% predicted reward) was subtracted from the ERP to no-reward feedback stimuli in the 0% reward probability condition (100% predicted no-reward) to generate a "predicted" difference wave (predicted feedback-RewP). Likewise, the ERP to reward feedback stimuli in the 75% reward probability condition (expected reward) was subtracted from the ERP to no-reward feedback stimuli in the 25% reward probability condition (expected no-reward) to generate an "expected" difference wave (expected feedback-RewP). The ERP to reward feedback stimuli in the 25% reward probability condition (unexpected reward) was subtracted from the ERP to no-reward feedback stimuli in the 75% reward probability condition (unexpected no-reward) to generate an "unexpected" difference wave (unexpected feedback-RewP). Finally, the ERP to reward feedback stimuli in the 50% reward probability condition (50% reward) was subtracted from the ERP to no-reward feedback stimuli in the 50% reward probability condition (50% no-reward) to generate a "50%" difference wave (50% feedback-RewP). Feedback-RewP amplitude was then determined by finding the maximum negative deflection in the difference wave from 200 to 320 ms (determined based on visual inspection of the feedback-RewP for each participant and condition) following feedback onset, separately for the predicted, expected, unexpected, and 50% feedback-RewP; this difference-wave approach isolates the interaction of expectancy with valence by removing the main effect of probability (Holroyd & Krigolson, 2007; Sambrook & Goslin, 2015). Consistent with previous studies, we expected the amplitude of feedback-RewP to scale with the expectation of reward probability, in keeping with a RPE signal, being largest when rewards are least expected (unexpected feedback-RewP), intermediate when rewards are random (50% feedback-RewP), smaller when rewards are expected (expected feedback-RewP), and smallest when rewards are completely predicted (predicted feedback-RewP) (Holroyd et al., 2003; Holroyd & Krigolson, 2007; Holroyd et al., 2009; Sambrook & Goslin, 2015).

I analyzed the three other ERP components at channel FCz, where they reached maximum amplitudes collapsed across conditions (but see below), but only for the last four blocks of both task phases (i.e., blocks 5 to 8 & blocks 13 to 16)[1], as I assumed that participants acquired the cue-response mappings in the latter half of each phase. First, the "cue-RewP" was measured within a time-window of 200-320 ms post-cue onset and analyzed with the difference wave approach (see below). Second, the SPN was measured as mean ERP amplitude from 600 ms before until the onset of feedback delivery, time-locked to cue onset. Third, the readiness potential was measured as mean ERP amplitude from 200 ms preceding response onset until response onset. In contrast to how I assessed the feedback RewP which was averaged according to feedback valence (reward, no reward) and then assessed as a difference wave, cue-RewP, SPN amplitude, and readiness potential amplitude were each averaged across feedback valence (reward, no reward), separately for each of the five reward probability conditions (i.e., these ERPs will be called "raw" ERPs for each reward probability condition to distinguish them from the ERPs assessed as difference waves, below). In addition, to conduct multiple regression analyses on the personality trait scores, I utilized a difference wave approach on cue-RewP, SPN, and readiness amplitude in order to equate the expectedness of rewards with "predicted" and "expected" difference waves as per above. Specifically, the ERP in the

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[1] This criterion was used for all the ERP components analyzed except for the reward positivity (which utilized a different learning criteria, see above). The different learning criterion for the RewP was used to increase the number of trials for averaging, which was of special concern for the unexpected RewP, which was associated with relatively fewer trials (note that the minimum number of trials for RewP were at least 5).

100% reward probability condition was subtracted from the ERP in the 0% reward probability condition to generate a “predicted” cue-RewP. The ERP in the 75% reward probability condition was subtracted from the ERP in the 25% reward probability condition to generate an “expected” cue-RewP. Further, as a control comparison, the ERP to the 50% reward probability was also analyzed such that the ERP preceding positive feedback was subtracted from the ERP preceding negative feedback, yielding a “50%” cue-RewP. The same procedure was applied to generate a “predicted” SPN and readiness potential, an “expected” SPN and readiness potential, and a “50%” SPN and readiness potential. Finally, each ERP component was also averaged across trials irrespective of the outcome probabilities, yielding an overall feedback RewP, an overall cue-RewP, an overall SPN, and an overall readiness potential.

All of the analyses were conducted using SPSS (IBM SPSS 23). A within-subject ANOVA with repeated measures was conducted on the amplitude of each of the ERP components, and a post-hoc contrast was used to assess the expected linearity as a function of reward probability. A multiple linear regression analysis was conducted separately on the amplitude of each ERP component with the personality traits as predictors, using the backward method in which all of the predictors were entered into the model first and then non-contributing predictors were step-wise eliminated (with the criterion that the minimum p-value for each personality trait to remain in a regression model was 0.1). Outliers were eliminated as described in the introduction.

Results

Two participants were removed from the analyses because they reported taking medications associated with psychosis and with seizures, and an anti-depressant. In total 66 participants were included in the analyses[2].

Questionnaires

Table 1 shows a summary of each questionnaire score, and Table 2 shows zero-order correlations among questionnaires.

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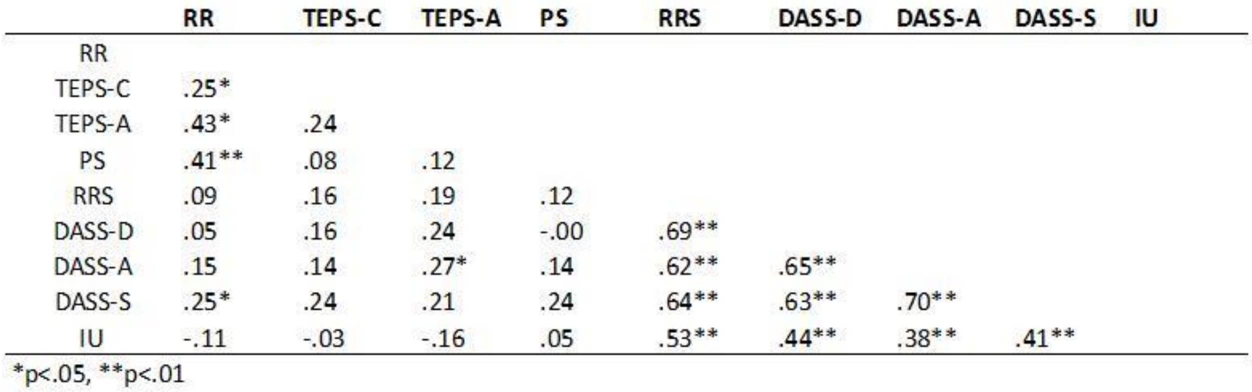
[2] Two participants on anti-depressant (Cipralex) were included in the analyses because excluding them did not change the obtained results.

	Mean	SD	Range
RR	26.4	2.7	20-32
TEPS-C	38.8	4.8	24-48
TEPS-A	45.9	5.6	26-60
PS	69.4	10.4	36-90
RRS	45.2	12.4	25-86
DASS-D	3.9	4.1	0-19
DASS-A	5	4.6	0-21
DASS-S	6.3	4.2	0-21
IU	29.5	9.4	16-59

Table 1. A summary of participants' questionnaire scores in Experiment 1. RR=reward responsiveness scale. TEPS-C=temporal experience of pleasure scale, consummatory pleasure subscale. TEPS-A=temporal experience of pleasure scale, anticipatory pleasure subscale. PS=persistence scale. RRS=ruminative responses scale. DASS-D=depression subscale of the depression, anxiety, stress scale (DASS-21). DASS-A=anxiety subscale of DASS-21. DASS-S=stress subscale of DASS-21. IU=intolerance of uncertainty scale.



	RR	TEPS-C	TEPS-A	PS	RRS	DASS-D	DASS-A	DASS-S	IU
RR									
TEPS-C	.25*								
TEPS-A	.43*	.24							
PS	.41**	.08	.12						
RRS	.09	.16	.19	.12					
DASS-D	.05	.16	.24	-.00	.69**				
DASS-A	.15	.14	.27*	.14	.62**	.65**			
DASS-S	.25*	.24	.21	.24	.64**	.63**	.70**		
IU	-.11	-.03	-.16	.05	.53**	.44**	.38**	.41**	

*p<.05, **p<.01

Table 2. Zero-order correlations among questionnaire scores.

Behavior

Accuracy and reaction times (RT) for each condition are shown in Figure 6. Note that the dip in accuracy at block 9 corresponds to the new set of stimulus cues at the start of Phase 2. Moreover, because the cue stimulus was presented for 800 ms before participants were allowed to make a response, relatively fast RTs across blocks likely indicate that participants prepared for the response early while the cue was still on the screen. A repeated-measures ANOVA on accuracy with reward probability as the within-subject factor revealed a significant effect of probability, F(3.4, 222)=180, p<.01, η_p^2=.74 (Greenhouse-Geisser corrected). Polynomial contrasts indicated a significant linear trend, F(1,65)=470.6, p<.01, η_p^2=.88, a quadratic trend, F(1,65)=94.4, p<.01, η_p^2=.59, and a cubic trend, F(1,65)=17.7, p<.01, η_p^2=.21. The same analysis on RT also revealed a significant effect of probability, F(3.4, 219)=16.8, p<.01, η_p^2=.21 (Greenhouse-Geisser corrected). Polynomial contrasts indicated a significant linear trend, F(1,65)=47.5, p<.01, η_p^2=.40, and a quadratic trend, F(1,65)=7.3, p<.01, η_p^2=.10. These results indicate that performance improved (i.e., higher accuracy and faster RT) as a function of increased reward probability. Zero order correlations revealed that persistence scores were correlated positively with overall accuracy (N=66, r=.25, p=.04), which was the case in the 75%, 50%, and 25% reward probability conditions (all p<.05). Depression scores on the other hand were correlated negatively with accuracy in the 25% reward probability condition (N=66, r=-.24, p=.05) (Figure 7).

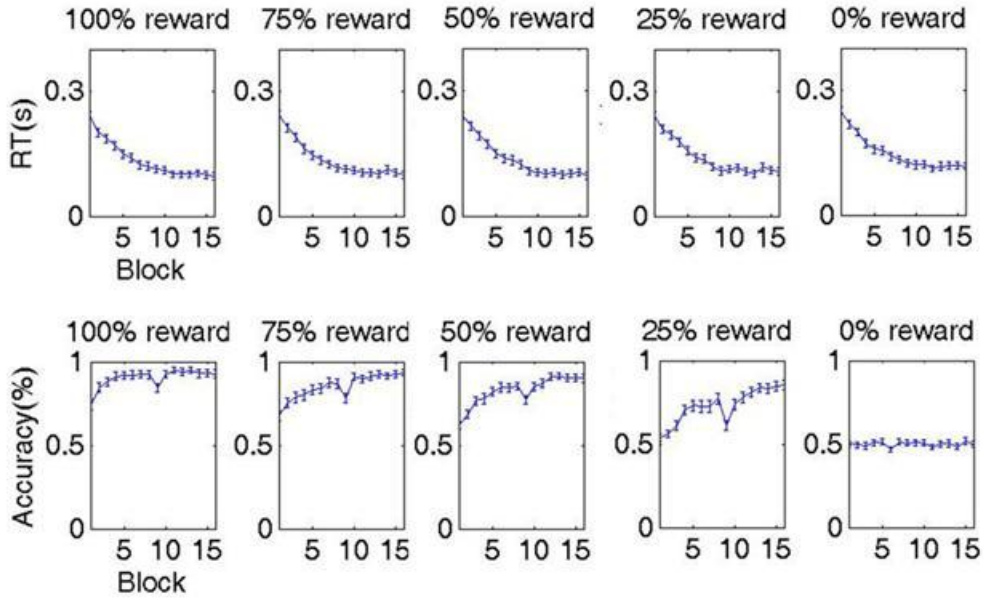


Figure 6. Block by block performance in reaction times (top) and accuracy (bottom) across different probabilities (from the 100% reward probability condition on the left to the 0% reward probability condition on the right). The x-axis indicates each block from block 1 to block 16 (new cues were introduced at the beginning of block 9). Error bars indicate standard errors of the means.

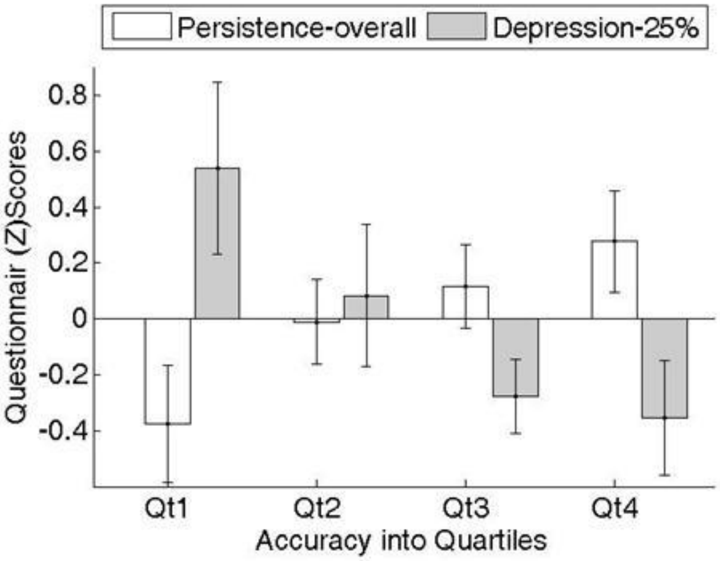


Figure 7. Performance accuracy sorted into quartiles in relation to persistence and depression scores. The x-axis shows accuracy for each quartile (Qt), with Qt1 associated with lowest accuracy and Qt4 associated with highest accuracy. Accuracy across the probabilities (100%, 75%, 50%, and 25%) was sorted into quartiles for the persistence scores (white bars), while accuracy for the 25% reward probability condition was sorted into quartiles for the depression scores (gray bars). The y-axis shows standardized questionnaire scores for persistence and depression scales. Error bars indicate standard errors of the means.

ERPs

Cue RewP. Figure 8 presents the entire time-course of ERPs time-locked to the onset of predictive cues. With respect to the cue-RewP, the amplitude at channel Cz was numerically larger, but it was not statistically different from FCz (p=.4), hence the analysis was conducted using the data recorded at channel FCz. A repeated-measures ANOVA with reward probability as a within-subject factor revealed a significant effect of probability, F(2,130)=9.7, p<.01, η_p^2=.13 (Figure 9a). The polynomial contrast indicated a linear trend, F(1,65)=16.1, p<.01, η_p^2=.20, such that the predictive cue-RewP was the largest (most negative), the expected cue-RewP was the second largest, and the

50% cue-RewP was the smallest (most positive), which is in line with the theory that the RPE signals propagate back in time with learning from feedback stimuli to events that predict the feedback (Baker & Holroyd, 2009; Holroyd, Krigolson & Lee, 2011; see also Holroyd & Coles, 2002). A multiple linear regression analysis on the overall cue-RewP amplitude (averaged across conditions) with the personality trait scores as predictors did not reveal a significant model. Table 3b lists a summary of the results of separate multiple linear regressions for each probability condition with personality trait scores as predictors.

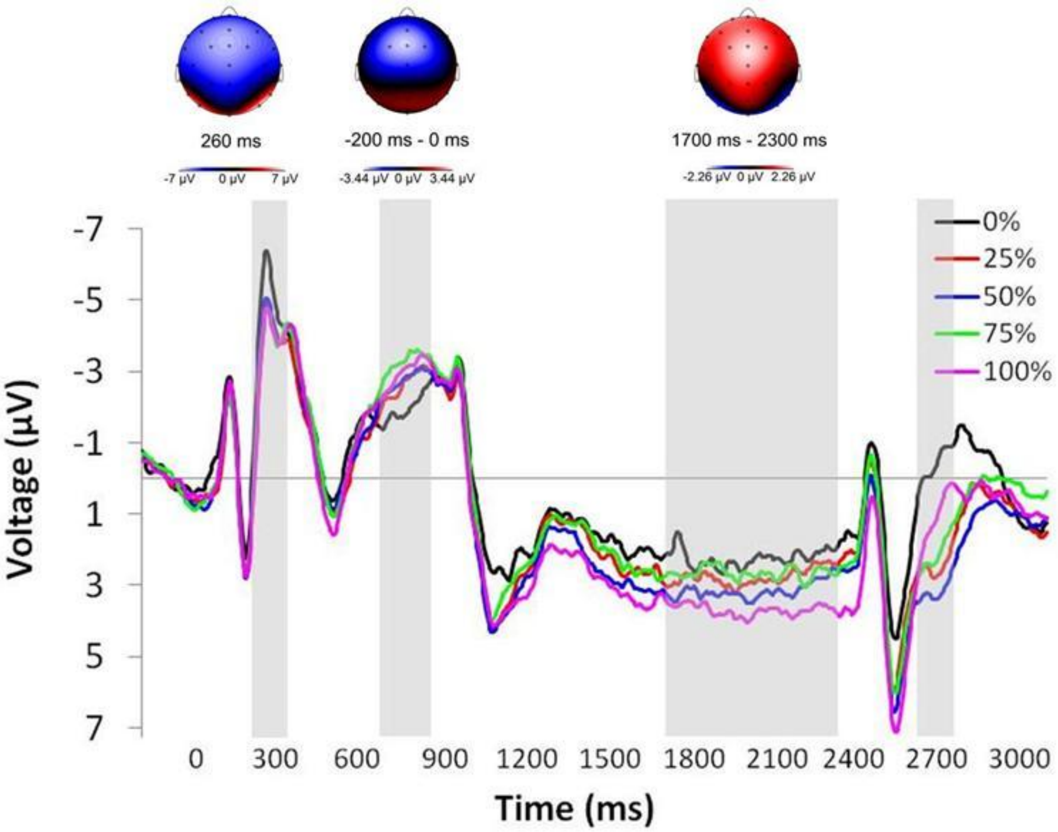


Figure 8. Event-related brain potentials (ERPs) and associated scalp voltage maps time-locked to the onset of predictive cues (at time 0ms) and measured at channel FCz. The five reward probability conditions are shown in different colors: 0% reward probability = black, 25% reward probability = red, 50% reward probability = blue, 75% reward probability = green, 100% reward probability =pink. Time periods of evaluation are shown for each ERP component in the grey shaded areas. The cue-RewP is evaluated between 200-320 ms, the readiness potential is evaluated immediately preceding response execution around 800 ms (the 2nd highlighted area from the left), SPN is evaluated during the 600 ms

interval preceding the onset of feedback stimulus between 1700-2300 ms, and the feedback RewP is evaluated around 2700 ms (the last highlighted area from the left). Note that because the readiness potential and the feedback-RewP were time-locked to the onset of response, which varied from trial to trial, and the onset of feedback stimuli, respectively, these components illustrated here are only approximate. The scalp voltage map for the cue-RewP (left-most), readiness potential (middle), and SPN (right-most) are shown over their associated period of evaluation. Negative is plotted up by convention.

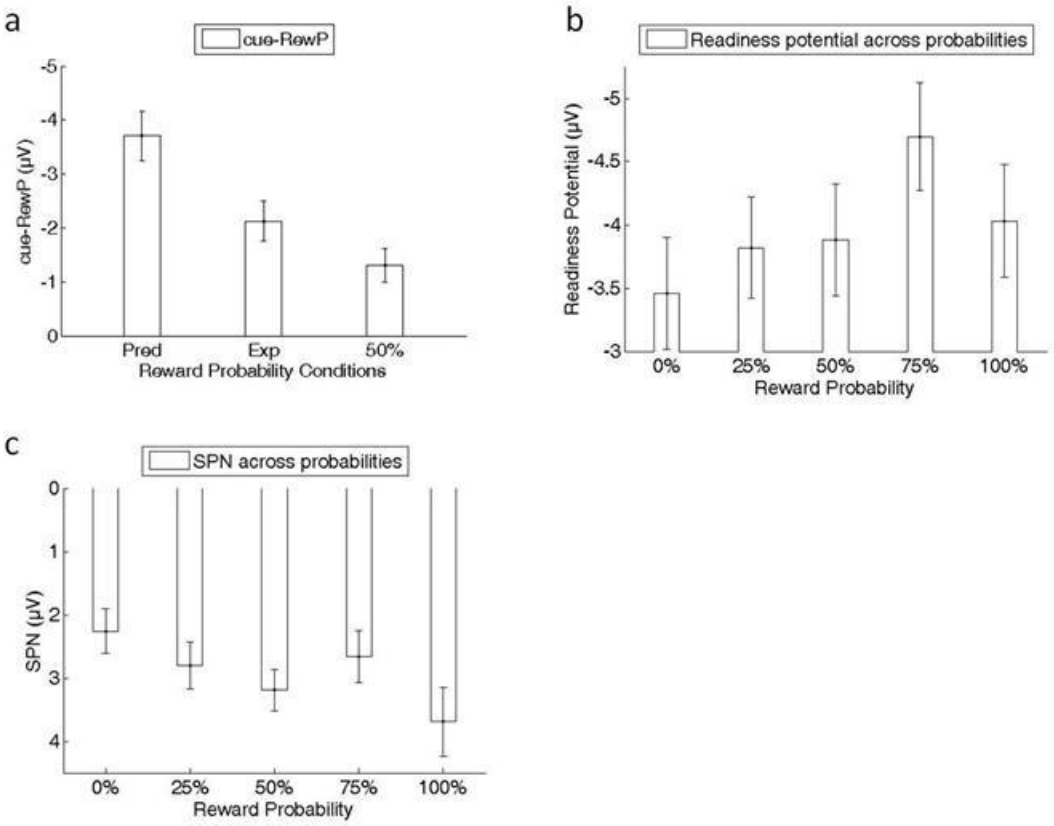


Figure 9. ERP components across conditions. (a) cue-RewPs for the predicted cue-RewP (Pred), the expected cue-RewP (Exp), and the 50% cue-RewP (50%). (b) Stimulus Preceding Negativity (SPN) and (c) readiness potential across reward probabilities (x-axis). The y-axis shows the voltage. Negative is plotted up to align with the ERP waveforms. Error bars indicate standard errors of the means.

(a)

Multiple linear regression for each ERP component **overall**

	Predictors	Beta	t	p	Final model	R^2
SPN	Depression	-0.35	-2.5	0.01	F(2,61)=3.5, p=.04	0.1
	IU	0.24	1.8	0.08		
Feedback-RewP	RR	-0.21	-1.7	0.1	F(1,63)=2.8, p=.1	0.04

(b)

Multiple linear regression on **cue-RewP** separately for each probability condition

	Predictors	Beta	t	p	Final model	R^2
Predicted cue	IU	0.31	2.6	0.01	F(1,64)=6.6, p=.01	0.09

(c)

Multiple linear regression on **readiness potential** separately for each probability condition

	Predictors	Beta	t	p	Final model	R^2
Predicted Rpot	RR	-0.29	-2	0.05	F(3,60)=3, p=.04	0.13
	TEPS-A	0.28	2.1	0.04		
	Persistence	0.26	2	0.05		
Expected RPot	Depression	-0.27	-2.2	0.03	F(1,64)=5, p=.03	0.07

(d)

Multiple linear regression on **SPN** separately for each probability condition

	Predictors	Beta	t	p	Final model	R^2
Predicted SPN	TEPS-A	0.28	2.2	0.04	F(3,61)=3, p=.04	0.13
	Depression	-0.25	-1.7	0.09		
	IU	0.37	2.6	0.01		

(e)

Multiple linear regression on **feedback-RewP** separately for each probability condition

	Predictors	Beta	t	p	Final model	R^2
Predicted RewP	RR	-0.27	-2.2	0.03	F(2,62)=3.8, p=.03	0.11
	Depression	0.21	1.8	0.08		
Expected RewP	TEPS-C	-0.29	-2.4	0.02	F(2,63)=4.4, p=.02	0.12
	Depression	0.26	2.1	0.04		

Table 3. A summary of multiple regression analyses conducted (a) across the probability conditions for each ERP component, and separately for each probability condition for (b) cue-RewP, (c) readiness potential, (d) SPN, and (e) feedback-RewP.

Readiness Potential. The readiness potential was measured immediately preceding response execution. A repeated measures ANOVA on the raw readiness potential amplitude with reward probability as a within-subject factor revealed a significant effect of probability, $F(3.4,220)=3.5$, $p=.01$, $\eta_p^2 = .05$ (Greenhouse=Geisser corrected). The polynomial contrast indicated a significant linear trend, $F(1,65)=4.6$, $p=.04$, $\eta_p^2=.07$, such that as the reward probability increased from 0% to 100%, the raw readiness potential became more negative (Figure 9b). A multiple linear regression analysis on the overall readiness potential amplitude (averaged across probabilities) with personality trait scores as predictors did not reveal a significant model. Table 3c provides a summary of the results of multiple regression analyses with personality traits as predictors performed separately for each probability condition (i.e., on the predicted and expected readiness potential). Of interest, expected readiness potential was larger (more negative) in participants high in depression scores. Figure 10 illustrates this result by comparing participants with the lowest depression scores with participants with the highest depression scores (averaged separately for the smallest and largest quartiles) for the 25% and 75% reward probability conditions. Participants high in depression scores produced a larger (more negative) raw readiness potential when rewards were unlikely (i.e., 25%) compared to when rewards were more likely (i.e., 75%), whereas participants low in depression scores showed the opposite pattern, with enhanced raw readiness potential when rewards were more likely (i.e., 75%) compared to when rewards were unlikely (i.e., 25%) (as was also observed across participants; Figure 9b).

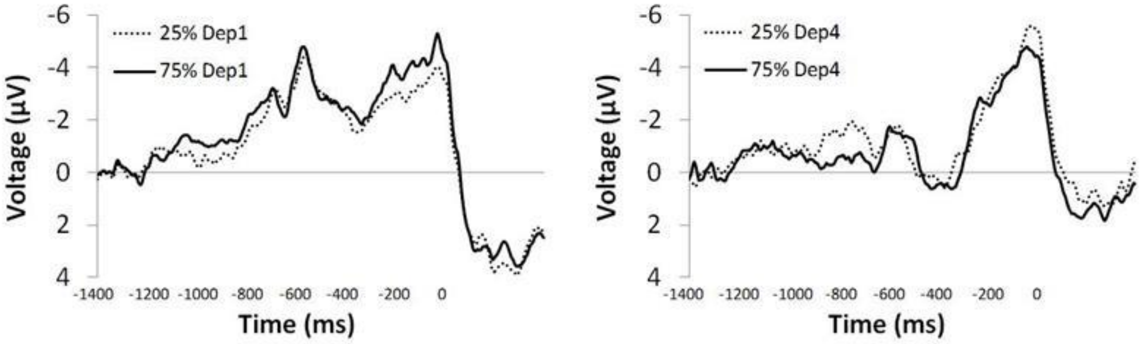


Figure 10. Event-related brain potentials (ERPs) time-locked to the onset of response (at 0ms) for participants lowest in the depression scores (Dep1) on the left figure and participants highest in the depression scores (Dep4) on the right figure. Readiness potential following the 25% (dotted line) and 75% (solid line) reward probability cues were measured

at FCz in the 200ms interval immediately before the response execution at time 0ms. Negative is plotted up by convention.

SPN. SPN was examined immediately preceding the receipt of the reward feedback (Figure 8). A repeated ANOVA on the raw SPN amplitude with reward probability as the within-subjects factor revealed a significant effect of probability, F(2.5,160)=3, p=.04, η_p^2=.05 (Figure 9c) (Greenhouse-Geisser correction applied). Polynomial contrasts indicated a significant linear trend, F(1,65)=5.7, p=.02, η_p^2=.08, and a cubic trend, F(1,65)=4.7, p=.03, η_p^2=.07 (Figure 9c). As suggested previously (see Fuentemilla et al., 2013), raw SPN appears to scale with the motivational state for gaining improbable rewards, such that as the rewards become less probable (i.e., from 100% to 0%), the raw SPN becomes more negative. Simple contrasts comparing the raw SPN amplitude for each probability condition to the raw SPN amplitude for the 100% probability condition, which served as a reference, indicated that the raw SPN was significantly more negative in the 0%, 25%, 75% probability conditions (all p=.01), but not in the 50% probability condition (p=.09). A multiple linear regression analysis on the overall SPN amplitude (averaged across probabilities) indicated that participants high in depression and low in IU scores produced larger (more negative) SPNs overall, F(2,61)=3.5, p=.04, explaining 10% of the variance (Table 3a). A summary of multiple linear regression analyses conducted separately for each probability condition is shown in Table 3d. Of interest, Figure 11 shows differences in predicted SPN between participants lowest and highest in IU based on quartiles. Between-group simple t-tests indicate that raw SPN was reduced (more positive) for both the 0% and 100% reward probability conditions (both p<.05) in participants highest in IU compared to participants lowest in IU.

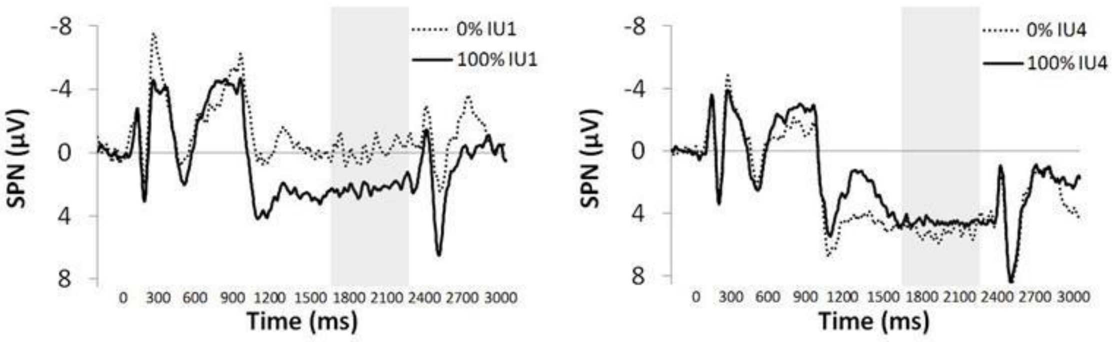


Figure 11. Event-related brain potentials (ERPs) time-locked to the onset of reward predictive cues (at 0ms) for participants lowest in intolerance of uncertainty (IU) (IU1) on the left figure and participants highest in the IU (IU4) on the right figure. Stimulus preceding negativity (SPN) is highlighted between 1700-2300 ms post cue onset following the 0% (dotted line) and 100% (solid line) reward probability cues, measured at FCz. Negative is plotted up by convention.

Feedback-RewP. To test the probability effect for the feedback-RewP, a repeated ANOVA on feedback-RewP amplitude with reward probability as a within-subject factor (i.e., predicted, expected, unexpected, and 50% feedback-RewP) was conducted, which revealed a significant effect of probability condition, F(2.6,167)=22.4, p<.01, η_p^2=.26 (Greenhouse-Geisser correction applied) (Figure 12). Polynomial contrasts indicated a significant linear trend, F(1,65)=37.1, p<.01, η_p^2=.36, and quadratic trend, F(1,65)=12.7, p<.01, η_p^2=.16. Further analysis revealed that predicted feedback-RewP was numerically, but not significantly, smaller than the expected feedback-RewP (p=.4), which was smaller than the 50% feedback-RewP, F(1,65)=3.7, p=.06, which was significantly smaller than the unexpected feedback-RewP, F(1,65)=26.5, p<.01, η_p^2=.28. Broadly consistent with previous observations, the feedback-RewP amplitude displayed an interaction of valence with expectancy (Holroyd & Krigolson, 207; Sambrook & Goslin, 2015).

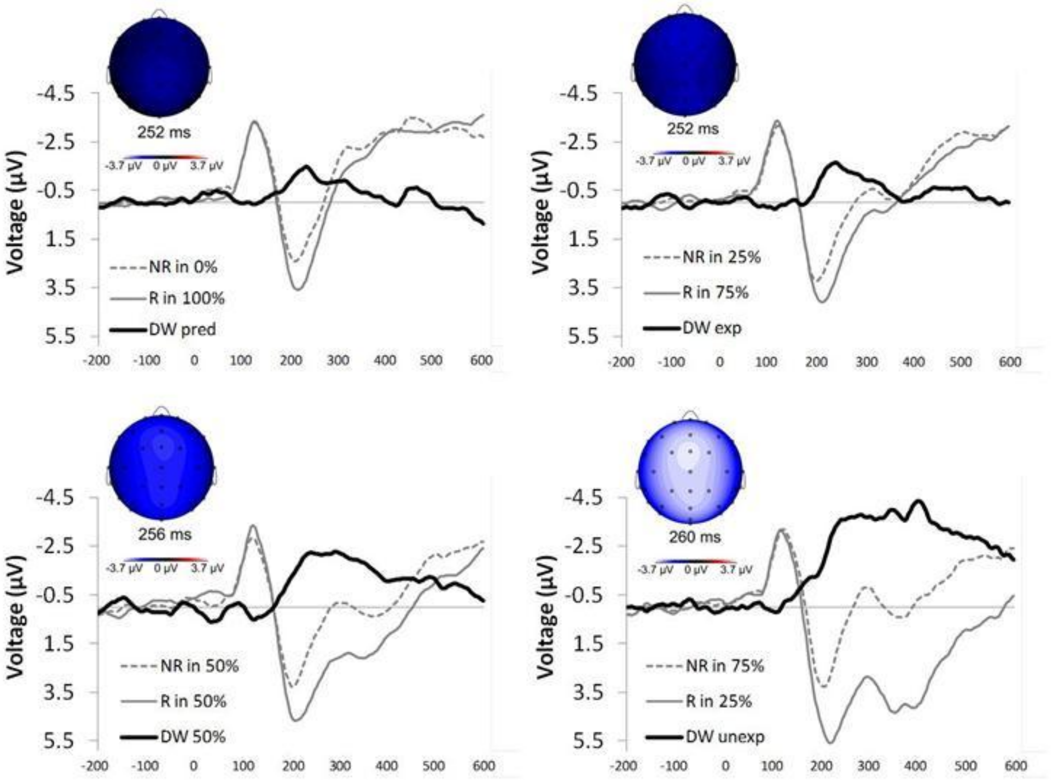


Figure 12. Event-related brain potentials (ERPs) and associated scalp voltage maps elicited time-locked to the onset of reward feedback (at 0ms). Feedback reward positivity (feedback-RewP) measured at FCz for each condition (negative is plotted up by convention). Difference waves (black) were calculated by the reward ERPs (gray line) subtracted from the no-reward ERPs (dotted gray line). Top left: Feedback reward positivity for the predicted condition elicited by the ERP to the no-reward feedback in the 0% reward probability condition (gray, dotted line) and to the reward feedback in the 100% reward probability condition (gray line). Top right: Feedback reward positivity for the expected condition elicited by the ERP to the no-reward feedback in the 25% reward probability condition (gray, dotted line) and to the reward feedback in the 75% reward probability condition (gray line). Bottom left: Feedback reward positivity for the 50% condition elicited by the ERP to the no-reward feedback in the 50% reward probability condition (gray, dotted line) and to the reward feedback in the 50% reward probability condition (gray line). Bottom right: Reward positivity for the unexpected condition elicited by the ERP to the no-reward feedback in the 75% reward probability condition (gray, dotted line) and to the reward feedback in the 25% reward probability condition (gray line).

A multiple regression analysis on the overall feedback-RewP (averaged across probability conditions, see above) indicated a trend that participants high in reward responsiveness produced a larger (more negative) overall feedback-RewP, F(1,63)=2.8, p=.1, explaining 4% of the variance in feedback-RewP amplitude (Table 3a). Table 3e provides a summary of multiple regression analyses conducted separately for each condition. The analysis indicates that participants high in reward sensitivity (i.e., reward responsiveness and consummatory pleasure) and low in depression scores produced a large feedback-RewP, particularly when rewards were highly expected.

Correlations between behavior and ERPs

Zero-order correlations were examined among the overall accuracy, RTs, and the four ERP components, averaged across reward probabilities. There was a marginally significant positive correlation across individuals between the overall accuracy and overall feedback-RewP (Pearson r=.23, p=.06), indicating that the feedback-RewP was smaller for people who performed the task better, likely due to increased expectancy for the feedback stimuli once the stimulus-response mappings were learned. Also, there was a trend for a positive correlation across individuals between the amplitudes of the overall cue-RewP and the overall SPN (Pearson r=.21, p=.09), indicating that reduced reward anticipation in response to reward predictive cues was associated with reduced reward anticipation in response to forthcoming feedback stimuli. The overall RTs did not correlate with overall readiness potential amplitude; however, note that the participants were able to prepare their response while the cue stimulus was still on the screen, such that the RT measure does not accurately reflect speed of processing, possibly accounting for this null result.

Discussion

Recent investigations on the neurobiological mechanisms of reward processing (Berridge et al., 2009; Schultz, 2007) have centered on understanding the relation between reward processing and depression, particularly as this relates to anhedonia (Der-Avakian & Markou, 2011; Pizzagalli, 2011, for review). Although anhedonia is classically associated with the inability to experience pleasure, more recent considerations have associated it with motivational deficits rather than to an inability to experience pleasure per se (Treadway & Zald, 2011). The evidence to date is inconclusive as to which reward processes are dysfunctional in individuals high in depression symptoms or depression-related traits. To investigate different aspects of reward processing, in the current study I recorded brainwaves from participants engaged in a reinforcement learning task in which they learned by trial and error specific cue-response associations that were most likely to elicit rewards. I then examined several ERP components in order to understand reward learning, anticipation, and outcome processing as these relate to individual differences in personality associated with ACC function.

Behaviorally, participants' task performance (in terms of both accuracy and RT) corresponded to reward probability, confirming that participants learned the stimulus-response mappings more easily for higher reward probabilities compared to lower reward probabilities. Moreover, participants who scored high in the trait persistence performed the task more accurately overall, while participants who scored high in depression performed the task worse, but only when the rewards were unlikely (i.e., following cues that predicted reward with 25% probability). This observation is consistent with previous findings that indicated that individuals with depression or with high levels of anhedonia fail to exhibit a response bias towards rewarding stimuli, especially with intermittent reward schedules (Kunisato et al., 2012; Pizzagalli et al., 2005; Pizzagalli et al., 2008), which has been said to reflect a difficulty with integrating reward history across trials (Pizzagalli et al., 2008). Conversely, given the putative association of persistence with the cognitive control process mediated by dACC, the high accuracy by persistent individuals in the present task might reflect a better ability to integrate rewards across many trials.

RPE signals carried by DA neurons are known to "travel back in time" with learning to the earliest indication of forthcoming reward (Schultz et al., 1997). A wealth of ERP studies suggest that a comparable process happens in humans (see Walsh & Anderson, 2012 for review). Accordingly, I expected to observe RPE signals elicited by the reward predictive cues, such that the reward predictive cues would serve as reward feedback once the cue-outcome relationships had been learned. As predicted, I found that the amplitude of the cue-RewP increased (i.e., became more negative) as the predictability of reward outcomes increased. Although there was no relation between the overall cue-RewP amplitude and individual differences in personality, participants high in IU produced a smaller cue-RewP to the predictive cue (i.e., the difference between the 0% and 100% reward probability condition). In view of the RPE theory of the reward positivity (Holroyd & Coles, 2002), the smaller RewP to the cue should be associated with an increased RewP to the feedback; however, this was not the case (see below).

I examined the readiness potential as an index of response preparation. Raw readiness potential amplitude increased (became more negative) as reward probability increased, indicating greater response preparation for behaviors that were most likely to result in reward. There was no correlation between the overall RTs and overall readiness potential, possibly due to the advance response preparation allowed while the cue stimulus was still on the screen. The raw readiness potential was also larger (more negative) in the 100% reward probability condition compared to the 0% reward probability condition (as revealed by the predicted readiness potential) in participants high in persistence and anticipatory pleasure but low in reward responsiveness. It is not clear why the predicted readiness potential was reduced in the latter group, but it may be that participants high in reward responsiveness viewed the unlikely rewards as being more likely (which would elicit a larger raw readiness potential on the 0% reward probability trials), or that they are primarily sensitive to reward acquisition (i.e., feedback-RewP) rather than to other aspects of reward processing (which would reduce the raw readiness potential on the 100% reward probability trials). Moreover, the raw readiness potential was larger (more negative) in the 75% reward probability condition compared to the 25% reward probability condition (as revealed by the expected readiness potential) in participants who scored low in depression. As illustrated in Figure 10, for participants who scored highest in depression (when grouped into quartiles), the amplitude of the raw readiness potential was larger in the 25% reward probability condition than in the 75% reward probability condition, which is the opposite pattern found for the people who scored lowest in depression. Given that participants high in depression scores were less accurate in the 25% reward probability condition, this finding may reflect their inability to discriminate between these conditions. Note also that inspection of Figure 10 suggests that the response preparation process also appears to start approximately 1 s later in participants highest in depression scores compared to participants lowest in depression scores. This may indicate that participants low in depression scores prepared their response in advance of the response execution period, whereas those high in depression scores were not able to do so, consistent with the poor accuracy observed in the 25% reward probability condition for the latter group.

I further examined reward anticipation with the SPN, which is characterized by a sustained negative potential over frontal-central areas of the scalp during the delay period prior to the delivery of reward feedback stimuli. Raw SPN amplitude increased (became more negative) as reward probability decreased, being largest in the 0% reward probability condition and the smallest (most positive) in the 100% reward probability condition. In contrast to a previous finding that found a linear relationship between raw SPN amplitude and reward probability (Fuentemilla et al., 2013), I also found a cubic trend in this relationship; the difference could possibly be due to a blocked design used in the previous study, in which different reward probability conditions were presented in separate blocks of trials rather than intermixed within the same block as was the case here. Nevertheless, the result appears to indicate that raw SPN is modulated by a level of expectancy associated with improbable positive outcomes, or alternatively with inevitable negative outcomes (Fuentemilla et al., 2013). Moreover, Fuentemilla and colleagues suggested that the anticipation of unlikely but desired rewards evoke emotional reactions, and observed that high risk-takers who exhibit intense emotional responses to highly wanted but unlikely rewards produced a larger (more negative) overall SPN compared to low risk-takers. Modulation of SPN amplitude by feedback stimuli inducing negative affect has also been observed previously; for example, anticipation of an aversive noise compared to a neutral tone elicited a larger SPN (Kotani, Hiraku, Suda, & Aihara, 2001), which aligns with the interpretation that inevitable negative outcomes elicit larger SPNs while expected positive outcomes elicit smaller (more positive) SPNs (see also Morís, Luque, & Rodríguez-Fornells, 2013).

In the present study participants high in depression scores and low in IU scores produced a larger (more negative) overall SPN. This finding may indicate heightened sensitivity to likely negative outcomes (i.e., a pessimistic view of the outcomes) by participants who scored high in depression. Moreover, the predicted SPN (the difference in raw SPNs between the 0% and 100% reward probability conditions) was larger in participants who scored high in depression compared to participants who scored low in depression, indicating that the former group highly differentiated the predicted forthcoming negative outcomes from the predicted forthcoming positive outcomes. By contrast, smaller (more positive) overall SPN in participants high in IU – who are characterized by excessive worry over unknown future events – may indicate a relatively more optimistic view of forthcoming rewards. However, when participants were grouped into quartiles according to their IU scores (see Figure 11) participants highest in IU produced raw SPNs in the 0% reward probability condition that was as small as in the 100% reward probability condition. It may be that participants high in IU are insensitive to or ignorant of completely predicted future outcomes (particularly, predicted negative outcomes) because of constant worry about future unknowns. This possibility aligns with the finding that participants high in IU also produced a smaller RewP to cues that were fully predictive of the outcomes, especially given that there was a trending positive correlation between the overall SPN and the overall cue-RewP in the present study, and both cue-RewP and SPN appear to broadly index reward anticipatory process. Moreover, the predicted SPN (the difference between the 0% and 100% reward probability conditions) was smaller in participants who scored high in anticipatory pleasure (i.e., TEPS-A), suggesting that these individuals may expect positive outcomes even when rewards are unlikely or impossible. Nevertheless, more investigations are necessary to elucidate what neurocognitive process SPN amplitude actually indexes.

I also examined the amplitude of the feedback-RewP as an indicator of reward sensitivity. As expected, feedback-RewP interacted with reward probability such that its amplitude increased (became more negative) as the reward outcomes became more unexpected. This result is the opposite of the effect of expectedness on cue-RewP amplitude, consistent with the theory that the reward signals propagate back in time with learning to the reward predictive cues (see above). Although the result exhibited only a statistical trend, participants high in reward responsiveness produced a relatively larger (more negative) overall feedback-RewP, which is consistent with a previous study (Bress & Hajcak, 2013; see also Liu et al., 2014). Moreover, participants high in reward sensitivity (as indicated by reward responsiveness and consummatory pleasure) and low in depression scores produced a larger feedback-RewP for rewards that were more probable. Although the relatively large feedback-RewP to highly probable rewards could indicate that the reward signals failed to propagate back with learning to their associated reward-predictive cues for these individuals, these traits were unrelated to the size of cue-RewP, and the result is also inconsistent with the finding that people high in depression scores were slower learners when rewards were unlikely (and thus should have produced a larger feedback-RewP to this condition). Moreover, participants with increased depression scores exhibited a relatively pessimistic view of forthcoming reward delivery as reflected in the relatively large (more negative) overall SPN; however, it was also unrelated to the size of feedback-RewP as this should have produced a larger feedback-RewP to (unexpected) positive outcomes. These findings therefore suggest that individual differences in feedback-RewP amplitude directly reflect individual sensitivity to reward value, rather than indirectly reflecting other aspects of the task such as differences in task performance.

Together these results point to impaired reward valuation in individuals high in depression symptoms rather than to impaired reward anticipation per se. The RewP is said to index the impact of RPE signals carried by midbrain DA neurons on to dACC (Holroyd & Coles, 2002; see also Walsh & Anderson, 2012). In turn, the RPE signals are produced in DA-innervated reward regions, particularly in the striatum (including nucleus accumbens) and connected brain areas such as the OFC. Impaired reward valuation by these regions, which are often seen to be hypoactive in depression, would result in the DA system carrying abnormal RPE signals to the dACC—as appears to be the case in individuals who exhibit multiple symptoms of depression.

Taken together, these results reveal a number of interesting findings that can be summarized as follows. First, persistent individuals exhibited a superior ability to integrate rewards across many trials, as revealed by better learning of response-outcome associations. Second, IU was associated with impaired reward anticipation, as revealed by a reduced cue-RewP and a reduced overall SPN, especially for highly predicted outcomes. As individuals high in IU are characterized by excessive worry about unknown events, they appear to ignore these predicted conditions. Third, participants high in depression scores performed worse for low probability reward trials while producing a larger raw readiness potentials on trials when rewards were unlikely compared to when they were more likely, which may indicate that participants high in depression scores were simply unable to discriminate between higher and lower reward predictive conditions. As noted above, this interpretation is partly consistent with the relatively delayed raw readiness potential in these conditions, indicating that participants high in depression scores were unable to prepare their response in advance compared to their counterparts. Although depression and IU scores were strongly correlated (see also, Nelson et al., 2014), depression symptoms were associated with more pessimistic assessment of reward delivery (as revealed by a larger overall SPN) and blunted reward sensitivity (as revealed by a smaller feedback-RewP), particularly when rewards were highly expected. As discussed above, the high expectation for negative outcomes and reduced reward learning in the low reward probability condition, coupled with a smaller feedback-RewP, is indicative of a primary deficit in reward valuation, as opposed to deficit in reward anticipation per se, which likely caused the deficit in reward learning.

Further, as observed in several previous studies (Proudfit, 2015), participants high in reward responsiveness produced relatively larger (more negative) feedback-RewP amplitudes, particularly when rewards were predicted; and the consummatory pleasure subscale of the anhedonia scale (i.e., TEPS) was correlated with larger feedback-RewP amplitude when rewards were expected, which is in line with the previous finding from healthy college students (Liu et al., 2014; but see also Cooper et al., 2014). Although the predicted association between the reward responsiveness trait and a larger RewP exhibited only a statistical trend, the weakness of the effect may be due to the learning involved in the present paradigm (see also footnote #3) compared to the simple guessing task used in previous studies (Bress & Hajcak, 2013). Moreover, participants high in reward responsiveness exhibited a relatively smaller difference in raw readiness potential amplitude between the predicted and unpredicted reward conditions (as revealed by the predicted readiness potential). The reason for this finding is less clear, but one possibility is that these participants viewed the unlikely rewards as being more likely. Alternatively, as noted above, it may indicate that the reward responsiveness trait primarily modulates responses to reward feedback and not to other reward-related processes. Strangely however, higher anticipatory pleasure was associated with an increased difference between these conditions (as revealed by the predicted readiness potential). Future studies should clarify the relationship between these reward sensitivity traits and neural mechanisms associated with response preparation. Finally, anticipatory pleasure was associated with a smaller (more positive) predicted SPN; although this result was opposite to what I had predicted, a post-hoc interpretation is that the participants high in anticipatory pleasure had an optimistic view of reward delivery even when rewards were not likely. Nevertheless, as TEPS is a relatively new anhedonia scale, more research is needed to investigate its relation to neural mechanisms of reward processing and to other reward sensitivity scales. For instance, it would be interesting to examine what aspect of reward responsiveness and TEPS-C was correlated with increased RewP, as these scales were reliably correlated with each other.

A limitation of the current study[3] is that the experiment involved only healthy college students, so the results might not generalize to clinically depressed individuals. Yet, it is promising that the amplitude of the feedback-RewP has been consistently associated with reward sensitivity both in sub-clinical and clinically depressed individuals (Foti et al., 2014; Liu et al., 2014). Moreover, reduced reward valuation as indicated by blunted feedback-RewP is already seen in pre-pubertal children and adolescents (Proudfit, 2015 for review). Nevertheless, blunted reward valuation as a biomarker for depression requires further investigation, as one recent study observed a normal feedback-RewP in depressed individuals who reported intact positive mood reactivity (Foti et al., 2014). Future studies examining individual differences in reward valuation are critically needed for advancing the current understanding of the etiology of depression.

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[3] Additionally, it is worth noting the task design regarding the 50% reward probability condition. In other tasks reward feedback is delivered with 50% probability irrespective of which response is chosen by the subject (e.g, Holroyd & Coles, 2002). For this reason the condition can control for individual differences in learning and performance on feedback-RewP amplitude; because the reward and no-reward outcomes are entirely unpredictable on such trials, they generate a feedback-RewP that is unconfounded by other task variables. However, on such trials in the present study the rewards were delivered with 50% probability following only one of the 2 responses, and were never delivered following the other response (Holroyd et al., 2009). Hence participants still had to learn the correct responses in this condition, and the no-reward outcomes occurred more frequently overall than the reward outcomes did. This nuance in the task design may explain why no association was found between the reward sensitivity scores (i.e., reward responsiveness, TEPS-C, and depression) and the 50% feedback-RewP as reported in previous studies, as well as for the remaining ERP components in this condition. Future investigations should take into account such differences in task design.

Although reward anticipation has been examined both in response to reward predictive cues and prior to reward delivery (see the introduction to this chapter), the present study indicated a link between depression and reward anticipation prior to feedback delivery (i.e., SPN). This suggests that participants high in depression scores were pessimistic about the probability of reward delivery, as revealed by an increased overall SPN. Although a link between SPN and dACC is not clear (but see below), past studies reporting increased dACC activity during reward anticipation may in part reflect this aspect of depression, which is highly sensitive to negative outcomes. For instance, these studies utilized tasks in which rewards were probabilistically delivered on about 50 to 66 % of the trials (Knutson et al., 2008; Gorka et al., 2014; Dichter et al., 2012; but see also Smoski et al., 2011), so the more depressed participants may have expected negative outcomes more than positive outcomes, inducing larger ACC activity. Furthermore, observations of a reduced fMRI BOLD response in dACC in depression may be due to collapsing different reward probability conditions across trials (Smoski et al., 2009). These observations also raise an important question about incorporating learning into tasks in order to examine reward processing (see Adams, Huys, & Roiser, 2016), as it has been widely acknowledged that the midbrain DA system is heavily involved in and dynamically impacts a variety of reward-related processes including reward learning (Berridge et al., 2009; Schultz, 2007).

Finally, it is worth noting that the severity or the clinical profile of depression may differentially impact reward anticipation, as previous studies have observed impaired reward anticipation only in individuals with chronic depression (i.e., early depression onset prior to adulthood; Nelson et al., 2014; Shankman et al., 2007; Shankman et al., 2013). Therefore, SPN amplitude may be modulated differently in individuals who exhibit such a clinical profile. Although most evidence points to anterior insular cortex as the primary generator of the SPN (see Böcker et al., 1994; Kotani, Ohgami, Ishiwata, Arai, Kiryu, & Inoue, 2015; Masaki, Yamazaki, & Hackley, 2010), a recent combined EEG and fMRI study using a time estimation task has revealed that other brain networks also contribute to the generation of SPN, including dACC (Kotani et al., 2015), which is consistent with a report that SPN is sensitive to dopaminergic modulation (Foti & Hajcak, 2012). As a link between reward anticipation and dACC has been indicated previously, future investigations elucidating the role of ACC in reward anticipation as it relates to SPN would be beneficial.

Experiment 2

The neurocognitive mechanisms that sustain task performance over long periods of time are poorly understood. The HRL-ACC theory proposes a key role for ACC in maintaining extended behaviors. This position is supported, for example, by an fMRI study involving a large number of participants in which dACC was activated throughout the execution of a wide variety of cognitive tasks (Dosenbach et al., 2006. See also Croxson et al., 2009). Likewise, lesion studies in monkeys (Amiez et al., 2006; Kennerley et al., 2006) and humans (Camille et al., 2011; see also Amiez, Champod, Wilson, Procyk, & Petrides, 2015) have reported that ACC damage causes an impairment in integrating the reward value of action outcomes across multiple trials, consistent with the position that ACC damage impairs the ability to sustain optimal performance over prolonged periods. Further, FMT, believed to be generated in the ACC, is generally regarded as a reliable neural signature of cognitive control and sustained mental effort (for reviews Cavanagh & Frank, 2014; Hsieh & Ranganath, 2014; Mitchell, 2008). FMT continuously rises throughout prolonged task performance (Barwick et al., 2012; Boksem et al., 2005; Wascher et al., 2014), suggesting that ACC supports sustained, effortful behavior in the face of increasing fatigue. Moreover, sustained task engagement is associated with a persistence-related personality trait (Tops & Boksem, 2010) which, in turn, has been associated with ACC function (Blanchard et al., 2015; Gusnard et al., 2003; Kurniawan et al., 2010; Parvisi et al., 2013).

In fact, motivational processes have been said to underlie mental fatigue, which has been related to the discrepancy between subjective costs of effortful behavior and potential rewards (Boksem & Tops, 2008). Inadequate maintenance of dopaminergic transmission to the striatum and ACC likely results in difficulties with sustaining behavior over time (Lorist et al., 2005), consistent with the putative role of the DA system in motivating behavior (Berridge, 2007; Dayan & Balleine, 2002). For instance, although increasing levels of fatigue can gradually impair task performance, sufficient motivation can counteract the effects of fatigue in order to sustain task performance (Kool & Botvinick, 2012; Sarter, Gehring, and Kozak, 2006; Westbrook & Braver, 2015), and can even restore performance after long, continuous episodes of cognitive work

(Boksem et al., 2006). It is worth noting that the level of cognitive or effortful control applied over task performance is not always observable in behavior. For instance, successful task performance can result either from a cognitively non-demanding task that requires little control, or from a cognitively demanding task that recruits sufficient levels of control. Likewise, the effect of reward valuation on behavior may not be obvious, particularly when a task requires individuals to accumulate rewards over time in order to obtain a long-term reward. Studies investigating the interaction between motivation and cognitive control have increased in recent years, and it has been argued that neural measures of control and reward valuation may provide distinct information about these processes that are independent of behavior (Botvinick & Braver, 2015 for review).

dACC is believed to serve as a computational hub that links motivation and control processes (Gläscher et al., 2012; Holroyd & Yeung, 2012; Shenhav et al., 2013; see Botvinick & Braver, 2015, for review). In line with this view, the HRL-ACC theory suggests that ACC utilizes the midbrain DA system's RPE signals to learn task values and to apply the appropriate degree of control over task performance, which is also consistent with a proposed role for DA in linking motivation and control (Aarts, van Holstein, & Cools, 2011). Further, it has been proposed that the two electrophysiological signatures of ACC, RewP and FMT, would reflect these processes: on this view, ACC utilizes the subjective reward valuation signal (as reflected in RewP amplitude) in order to apply sufficient control over task performance (as reflected in FMT), which sustains effortful behavior (cf. HajiHosseini & Holroyd, 2013; Holroyd, HajiHosseini & Baker, 2012). Moreover, the impact of motivation on cognitive control varies across individuals in ways that depend on individual differences in effort (Westbrook, Kester, & Braver, 2013) and reward (e.g., Braem, Verguts, Roggeman, & Notebaert, 2012; Engelmann, Damaraju, Padmala, & Pessoa, 2009; Locke & Braver, 2008) sensitivity. These observations are in line with past studies showing that individual differences in reward sensitivity and anxiety modulate RewP amplitude (see introduction) and FMT power (Mitchell et al., 2008; Cavanagh & Shackman, 2015), respectively.

However, individual differences in sustained behavior -- which according to the HRL-ACC theory is the cardinal function of ACC -- have not been well-investigated, especially as the subject relates to depression. One study suggested that patients with depression have difficulty sustaining positive emotions (but not negative emotions) over time, as indicated by reduced fronto-striatal brain activation (Heller et al., 2009). This observation is consistent with the clinical feature of depression that depression is characterized by sustained negative affect and/or reduced positive affect (i.e., anhedonia), as well as an inability to concentrate (APA, 2013). However, it remains to be tested whether individuals high in depression symptoms have difficulty sustaining effortful, goal-directed behaviors due to impaired control. This possibility is highlighted by the link between depression and ACC dysfunction, particularly as it is understood from the perspective of the HRL-ACC theory.

Here I investigated the role of ACC in sustaining task performance for a prolonged period of time and examined the relationships between particular personality traits and extended task performance. To do so, I employed a standard time estimation task that is commonly used to elicit the RewP, in which participants' brainwaves were recorded while they estimated 1 second on each trial. The participants were required to perform this simple task for 2 hours, and I examined the two neural signatures of ACC, the RewP and FMT, in relation to personality traits related to motivation and reward sensitivity that have been implicated in depression. I predicted that these neural markers would provide independent sources of information regarding individual differences in task performance. Another ERP component that is believed to reflect attentional process, the P300, was also investigated (Donchin & Coles, 1988; Polich & Kok, 1995). P300 is a large positive-going deflection that occurs to task-relevant unexpected events. The P300 follows the RewP in tasks with feedback, in the time range of about 300 to 500 ms following feedback presentation. This ERP component is said to reflect the amount of attentional resources allocated to a given stimulus (Isreal, Chesney, Wickens, & Donchin, 1980), therefore, I predicted that the P300 amplitude would decrease with time on task, indicating a continuous reduction in participants' task engagement.

Materials and methods

Participants

Sixty five undergraduate students were recruited from the University of Victoria Department of Psychology subject pool to fulfill a course requirement or earn bonus credits. All subjects (16 males, 10 left-handed, age range=17-23 years, mean age =19.3 +/- 1.5 years) had normal or corrected-to-normal vision. Each also received a monetary bonus in addition to the credits, the amount of which depended on their task performance (see below). All subjects provided informed consent as approved by the local research ethics committee. The experiment was conducted in accordance with the ethical standards prescribed in the 1964 Declaration of Helsinki.

Task Design

Participants were tested in the same environment as in Experiment 1 (see Task Design for Experiment 1). I utilized a time estimation task that required the participants to estimate 1 second on every trial (Miltner et al., 1997). Each trial started with presentation of a white central fixation cross (1 cm by 1 cm) in the center of the computer screen. Participants were instructed to press a left button on a computer mouse using their right hand when they believed that 1 second had elapsed following cue onset. 600 ms following the response, they were presented with a feedback stimulus indicating that their response was either on-time or not on-time. The response was considered on-time if it occurred within a narrow window of time centered around 1 second, the size of which was adjusted from trial to trial according to a staircase procedure, as follows. At the start of the experiment the size of the window was initialized at 200 ms, such that responses occurring between 900 and 1100 ms were considered correct. The size of the time window was then adjusted depending on the participant’s performance: error responses caused the time window to increase by 10 ms (making the task easier), and correct responses caused the time-window to decrease by 10 ms (making the task harder). This manipulation ensured that participants received reward feedback on approximately 50% of the trials (Miltner et al, 1997). The feedback stimuli were represented by abstract symbols presented at fixation (3.5 cm by 3.5 cm). For half of the participants, a white circle indicated that they would receive 1 cent for that trial at the end of the experiment, and a white diamond indicated that they would receive no reward for that trial. This mapping was reversed for the other half of the participants. After a variable ITI of 1400 ms, 1500 ms, or 1600 ms, determined at random, the next trial began with a presentation of the visual cue.

Further, we offered an additional motivational incentive to enhance individual differences in task performance by providing all of the participants an opportunity to participate in a lottery to win a CAN$100 Amazon.com gift card. Every participant earned at least 1 “ticket” regardless of their performance, which ensured that all subjects had at least a small chance of receiving the prize. In addition, the participants were told (truthfully) that the better performers would earn extra tickets. To be specific, participants received an extra ticket for every 5 ms decrement of their average time-window size with respect to the average time-window size across all participants. For example, an individual average time-window that was 15 ms less than the across-participant average would earn that participant 4 tickets total (3 additional tickets plus the baseline 1 ticket). Upon completing the experiment, all of the tickets were entered into a metaphorical lottery box, from which we randomly selected 2 winning participants. The two winners were presented with the award via email a few months after participating in this study.

Task Procedure

Before the experiment was described to them, all of the participants were asked to read a permission form that explained the opportunity to win a CAN $100 Amazon gift card. They were told that if they decided to consent to participate in the lottery then at least one ticket would be entered in their name into the lottery, and that additional tickets would be entered if their overall performance was better than the average performance across all of the participants. Consent was indicated by providing a contact email address on the form; only two participants did not provide consent.

Participants were then provided with both written and verbal instructions about the time estimation task. They practiced the task for 20 trials before starting the task proper, which consisted of 16 blocks of 95 trials each. Participants were not informed about the exact number of trials or blocks to complete, but instead were told that they would perform the task for about 2 hours. Self-paced between-block rest periods were provided, and after about 1hour participants relaxed during a longer rest period while the experimenter checked the electrode impedances. Participants were told that the reward they accumulated across trials would be paid out to them at the end of the experiment, and that they should estimate 1 second on each trial as accurately as possible in order to maximize their reward earnings. Upon completing the experiment they answered several personality questionnaires (see below). These were followed by a post-experiment paper-and-pen questionnaire that asked about the participant's overall experience of the experiment, the strategies they employed (if any), and their level of task engagement on a scale of 1 to 5, with 1 indicating not at all engaged and 5 indicating very engaged.

Questionnaires

The personality questionnaires administered included the Persistence Scale (Cloninger et al., 1993), the Ruminative Responses Scale (Nolen-Hoeksema et al., 1994), the Reward Responsiveness Scale (Van den Berg, Franken, & Muris, 2010), the Temporal Experience of Pleasure Scale (TEPS), (Gard, Gard, Kring, & John, 2006), and the Depression Anxiety Stress Scale (DASS-21) (Lovibond & Lovibond, 1995) (see Experiment 1 for details of each questionnaire). In addition, the 18-item Apathy Evaluation Scale (AES; Marin, Biedrzycki, & Firinciogullari, 1991) was included, which measures lack of motivation regarding the behavioral, cognitive, and emotional aspects of goal-directed behavior. The AES was coded on a scale from 1 (very characteristic) to 4 (not at all characteristic), such that higher total scores indicate higher levels of apathy. Because the DASS-21 depression subscale is often strongly correlated with the DASS-21 stress subscale and with RRS, which are not the primary focus of this study, these two questionnaires were not included in the analyses.

EEG Data Acquisition and Pre-processing

EEG data acquisition and pre-processing steps were identical to Experiment 1, except that the data were filtered offline with a passband of 0.10–30 Hz[4].

Data Analysis

Behavior

An average time-window size (TWS) was calculated for each participant by averaging the TWS across all trials. Therefore, smaller and larger average TWSs indicate

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[4] The range of the offline filter was widened with respect to Experiment 1 in order to conduct time-frequency analysis on the data.

better and worse performance, respectively. To examine changes in task performance between the 1st half and the 2nd half of the experiment, a performance ratio was calculated by taking the difference between the 1st and the 2nd half TWS (i.e., the 2nd half minus the 1st half TWS) divided by their sum (the sum of the 2nd and the 1st TWS), such that a positive ratio indicates worse performance (i.e., an increase in TWS) in the 2nd half compared to the 1st half of the experiment.

Electrophysiology

All details of the data analysis procedure are identical to Experiment 1 except where indicated otherwise. To note, ERPs were averaged across trials according to feedback type (reward, no-reward).The RewP was measured at channel FCz, where it reaches maximum amplitude (see below), utilizing a difference wave approach that isolated the reward positivity from overlapping ERP components such as the P300 (Holroyd & Krigolson, 2007; Sambrook and Goslin, 2015); a difference wave was created for each participant by subtracting the ERP to reward feedback stimuli from the ERP to no-reward feedback stimuli. RewP amplitude was then determined by finding the maximum negative deflection in the difference wave from 200 to 320 ms following feedback onset (determined based on visual inspection of the ERPs for each participant, which ensured that the window contained the maximum negativity across all participants). For the purpose of comparison, P300 amplitude was measured at channel Pz, where it typically reaches maximum amplitude across the scalp (Donchin & Coles, 1988), from individual subject ERPs that were averaged across feedback conditions by finding the maximum positive deflection from 280 to 420 ms following feedback onset. In order to assess FMT, the continuous EEG data were segmented into consecutive 4 seconds epochs (starting from the beginning of the experiment and continuing to the end) averaged across feedback types. Artifact rejection and ocular correction were conducted on these EEG epochs as for the ERP data, and then submitted to a power spectral analysis using a Fast Fourier Transform (FFT) (Hanning Window, 10% length). FMT was assessed for each trial by averaging power between 4 and 8 Hz at each channel. To examine changes in neural activity over time a ratio was calculated, separately, for RewP, P300, and FMT between the 1st half and the 2nd half of the experiment as was done for the TWS, above. A negative ratio indicates larger (more negative) RewP and a positive ratio indicates larger (more positive) P300 and FMT in the 2nd half compared to the 1st half of the experiment.

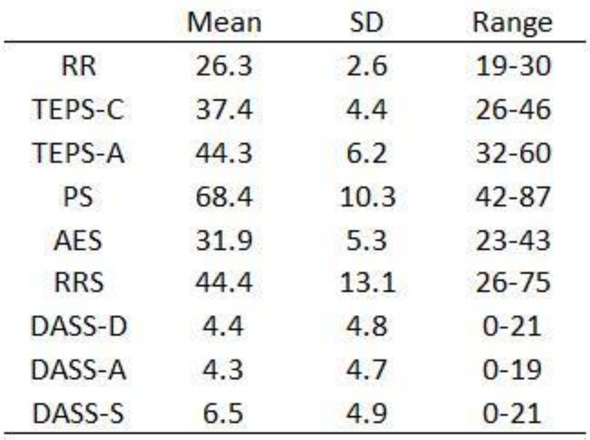
All of the analyses were conducted using SPSS (IBM SPSS 23). A within-subject ANOVA with repeated measures was conducted to examine changes in performance and neural activity (i.e., TWS, RewP, P300, and FMT) over time by experiment quarters. Multiple linear regression analyses were performed using the same method as in Experiment 1. The influence of outliers was trated accordingly to the jackknife procedure discussed in the introduction.

Results

Three participants discontinued the task (one participant indicated signs of claustrophobia and discontinued after completing one block of trials, one participant left feeling unwell, and one participant discontinued after reporting that s/he had earned enough money). The data of three other participants were excluded from analysis due to self-reported neurological or psychiatric disorders. Further, during the first few blocks of trials one participant produced extreme estimates of 1 second (of about 7 seconds); performance for this participant improved thereafter, but the probability of reward was strongly biased across blocks of trials due to the staircase procedure (i.e., mostly no reward in the first few blocks, followed by mostly reward in the remaining blocks). The data of two participants were also excluded due to artifacts associated with excessive head movement. In total these exclusions resulted in the data of 58 participants used for all of the analyses, except for analyses in which the data were separately averaged for each quarter of the experiment, which resulted in the data 57 participants for the ERP analysis and 56 participants for the FFT analysis. The number of participants included in each analysis is reflected in the degrees of freedom of the associated statistical tests.

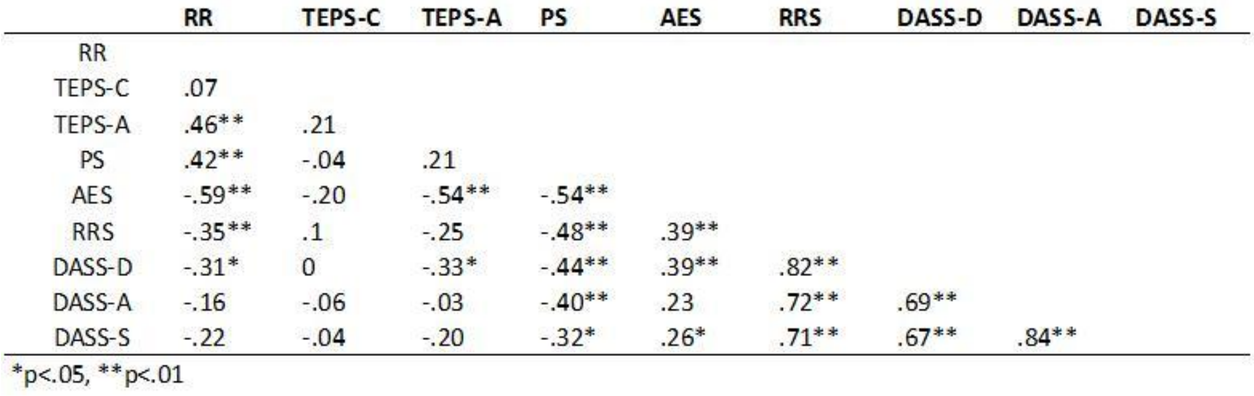
Questionnaires

A summary of each questionnaire score is provided in Table 4, and zero-order correlations among questionnaires are provided in Table 5.



	Mean	SD	Range
RR	26.3	2.6	19-30
TEPS-C	37.4	4.4	26-46
TEPS-A	44.3	6.2	32-60
PS	68.4	10.3	42-87
AES	31.9	5.3	23-43
RRS	44.4	13.1	26-75
DASS-D	4.4	4.8	0-21
DASS-A	4.3	4.7	0-19
DASS-S	6.5	4.9	0-21

Table 4. A summary of participant questionnaire scores in Experiment 2. AES=apathy evaluation scale. For other abbreviations, see Table 1.



	RR	TEPS-C	TEPS-A	PS	AES	RRS	DASS-D	DASS-A	DASS-S
RR									
TEPS-C	.07								
TEPS-A	.46**	.21							
PS	.42**	-.04	.21						
AES	-.59**	-.20	-.54**	-.54**					
RRS	-.35**	.1	-.25	-.48**	.39**				
DASS-D	-.31*	0	-.33*	-.44**	.39**	.82**			
DASS-A	-.16	-.06	-.03	-.40**	.23	.72**	.69**		
DASS-S	-.22	-.04	-.20	-.32*	.26*	.71**	.67**	.84**	

*p<.05, **p<.01

Table 5. Zero-order correlations among questionnaire scores.

Behavior

The average TWS across participants was 285ms (+/-109ms). A repeated ANOVA on TWS by experiment quarters (i.e., quarter1=block 1 through 4, or roughly the first 30 min, quarter 2= block 5 through 8, or roughly the next 30 min, etc) revealed a marginally significant effect of quarter, F(2, 110)=2.7, p=.08, η_p^2=.05 (Greenhouse-Geisser corrected). The polynomial contrast indicated a significant quadratic trend, F(1,56)=4.5, p=.04, η_p^2=.07, such that the TWS decreased until the 3rd quarter but increased in the last quarter (Figure 13a). The results of the post-experiment questionnaire revealed that higher levels of task engagement were correlated with better (smaller) TWS (Pearson r=-.28, p=.04), higher reward responsiveness scores (r=.30, p=.03), higher persistence (r=.31, p=.03), and somewhat reduced apathy (r=-.26, p=.06).

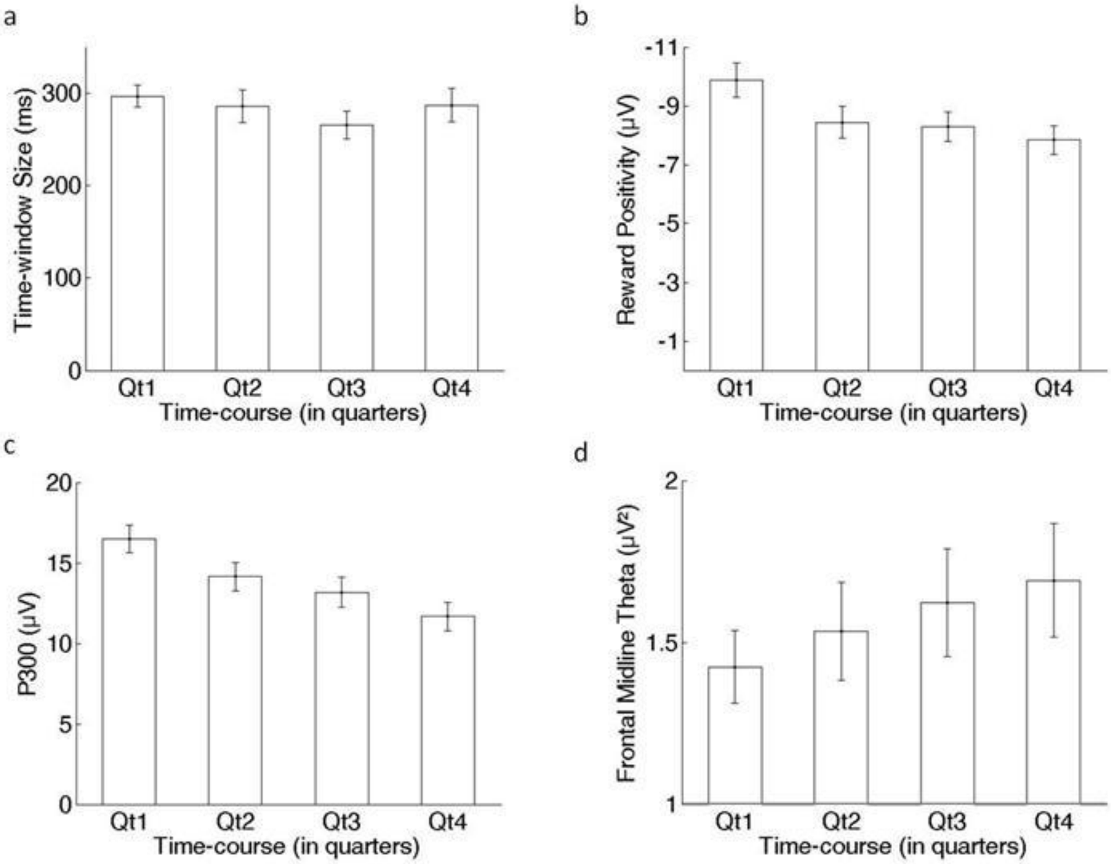


Figure 13. Quarter by quarter performance for (a) time-window size, (b) reward positivity (RewP) (negative is plotted up to align with the associated brainwaves), (c) P300, and (d) frontal midline theta (FMT). Qt1=blocks 1 to 4, Qt2=blocks 5 to 8, Qt3=blocks 9 to 12, Qt4=blocks 13 to 16. Error bars indicate standard errors of the means.

Electrophysiology

RewP: Figure 14 shows RewP averaged across trials for the entire experiment (Figure 14a) and the associated scalp voltage map (Figure 14b). A repeated ANOVA on RewP amplitude by experiment quarters revealed a significant effect of quarter, F(3, 168)=12.3, p<.01, η_p^2=.18 (Figure 14c). Post-hoc analysis indicated a significant linear trend, F(1,56)=24.7, p<.01, η_p^2=.31, such that RewP decreased (i.e., the difference wave became more positive) with time on task (Figure 13b).

P300: A comparable analysis on P300 amplitude revealed a significant effect of quarter F(2.2, 123)=49.2, p<.01, η_p^2=.47 (Greenhouse-Geisser corrected) (Figure 14d). There was a significant linear trend, F(1,56)=82, p<.01, η_p^2=.59, such that P300 decreased with time on task (Figure 13c).

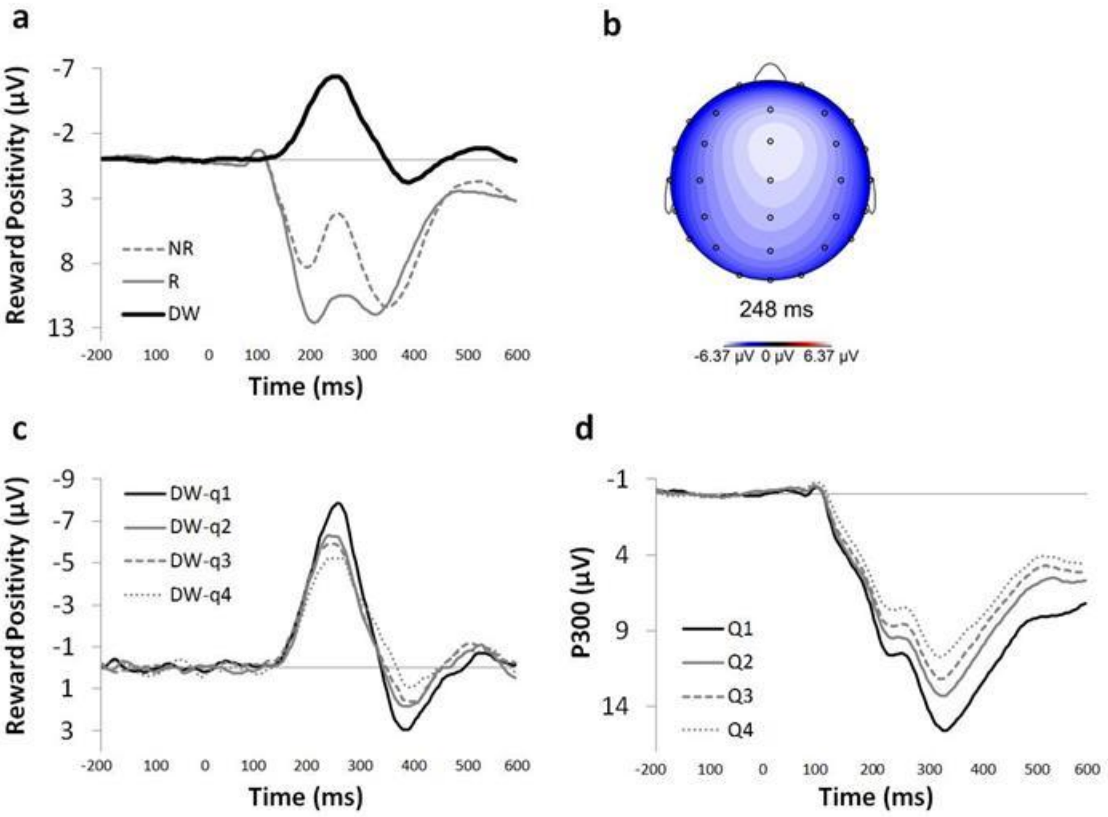


Figure 14. Event-related brain potentials (ERPs) elicited time-locked to the onset of reward feedback (at 0ms). The x-axis indicates time (ms). The y-axis indicates ERPs in voltage (µV). (a) Reward positivity (RewP) measured at FCz. Difference waves (DW: black) were calculated by the reward ERPs (R: gray line) subtracted from the no-reward ERPs (NR: dashed gray line). (b) Voltage distribution for RewP at the maximum negativity. (c) RewP (difference waves) for each quarter: DW-q1= RewP in quarter 1 (i.e., blocks 1 to 4). DW-q2= RewP in quarter 2 (blocks 5 to 8). DW-q3= RewP in quarter 3 (blocks 9 to 12). DW-q4= RewP in quarter 4 (blocks 13 to 16). (d) P300 measured at Pz for each quarter (same as in

RewP). Q1=quarter 1, Q2=quarter 2, Q3=quarter 3, Q4=quarter 4. Negative is plotted up by convention.

FMT: A repeated ANOVA on FMT power with experiment quarters as a within-subject factor revealed a significant effect of quarter, F(1.3,72)=12.1, p<.01, η_p^2=.18. Post-hoc analysis indicated a significant linear trend, F(1,55)=15.3, p<.01, η_p^2=.22 (Figure 13d).

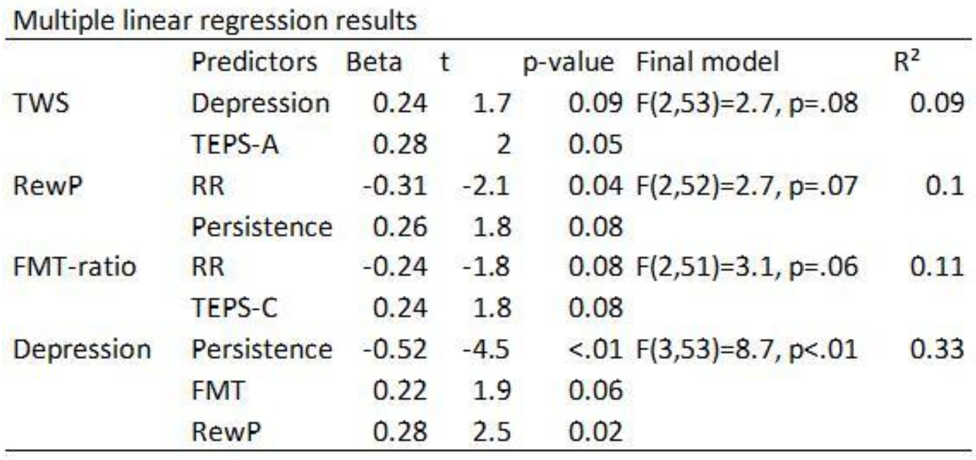
Correlations among measures

Behavior and electrophysiology correlations

Correlations of TWS with RewP amplitude (Pearson r = .30, p=.02) and P300 amplitude (Pearson r = -.42, p<.01) were both statistically significant, indicating that good performers produced larger RewPs and P300s. Partial regression indicated that the P300 correlation remained statistically significant when controlling for RewP amplitude (Person r = -.34, p=.01), but the converse was not true: The RewP correlation did not remain statistically significant when controlling for P300 amplitude (p=.3), indicating that the differences in performance across individuals were more closely related to variance in P300 amplitude than RewP amplitude. To investigate these findings further, exploratory post-hoc analyses indicated that there was no difference in RewP amplitude between the best performers (quartile 1) and the worst performers (quartile 4) (p>.5), whereas P300 amplitude was significantly larger (more positive) for the best performers compared to the worst performers (t(26)=2.6, p=.02). FMT was not correlated with any of these measures (all p>.5).

Behavior and personality traits correlations

A multiple regression analysis on TWS yielded a statistical trend suggesting that participants high in depression scores and TEPS-A performed the task worse, F(2,53)=2.7, p=.08, explaining 9% of the variance (Table 6). A multiple linear regression analysis conducted on the TWS ratio (see methods) did not reveal a significant model.



Multiple linear regression results

	Predictors	Beta	t	p-value	Final model	R²
TWS	Depression	0.24	1.7	0.09	F(2,53)=2.7, p=.08	0.09
	TEPS-A	0.28	2	0.05		
RewP	RR	-0.31	-2.1	0.04	F(2,52)=2.7, p=.07	0.1
	Persistence	0.26	1.8	0.08		
FMT-ratio	RR	-0.24	-1.8	0.08	F(2,51)=3.1, p=.06	0.11
	TEPS-C	0.24	1.8	0.08		
Depression	Persistence	-0.52	-4.5	<.01	F(3,53)=8.7, p<.01	0.33
	FMT	0.22	1.9	0.06		
	RewP	0.28	2.5	0.02		

Table 6. A summary of multiple linear regression results.

Electrophysiology and personality correlations

A multiple linear regression analysis on RewP amplitude yielded a statistical trend suggesting that participants high in persistence and low in reward responsiveness exhibited reduced (more positive) RewP amplitude, F(2,52)=2.7, p=.07, explaining 10% of the variance (Table 6). A comparable analysis on P300 amplitude did not reveal a significant model. Multiple regression analyses on the ratio between the 1st half and the 2nd half for RewP and P300 did not reveal significant models. A multiple linear regression analysis on FMT with the individual personality scores serving as predictors did not reveal any significant predictors of the overall FMT. A multiple linear regression analysis on the FMT ratio between the 1st and the 2nd half of the experiment indicated a trend that participants high in reward responsiveness and low in consummatory pleasure produced less FMT in the last compared to the 1st half of the experiment, F(2,51)=3.1, p=.06, explaining 11% of the variance (Table 6).

RewP, FMT, and personality

To understand the link between ACC function and associated personality traits, I conducted the following exploratory analysis. First, the two electrophysiological signatures of ACC function, RewP and FMT, were found to be uncorrelated with each other (Pearson r = .06, p=.64), indicating that they index distinct ACC-related processes (Figure 15). The finding that these measures are uncorrelated raises the question of whether their combined expression can better account for individual differences in personality traits related to ACC function. To investigate this possibility, I median-split the data along each dimension, resulting in four groups of individuals: the first group was characterized by small RewP and low FMT (“R1F1”, n=16), the second group by small RewP and high FMT (“R1F2”, n=13), the third group by large RewP and low FMT (“R2F1”, n=13), and the fourth group by large RewP and high FMT (“R2F2”, n=16). After standardizing the individual questionnaire scores across participants with z-scores, separately for each questionnaire, the pattern of personality traits was then examined separately for each group as shown in Figure 16. One-sample t-tests (two-tailed) were conducted for each quadrant, revealing the following. First, participants with small RewP and low FMT were characterized by a trend for high persistence (.36 +/- .81), t(15)=1.8, p=.1. Second, participants with small RewP and high FMT were characterized by a trend for high anxiety scores (.58 +/- 1.25), t(12)=1.7, p=.12. Third, participants with large RewP and low FMT were characterized by low depression scores (-.44 +/- .52), t(12)=-3.1, p=.01,and a trend for high reward responsiveness (.44 +/- .78), t(12)=2, p=.07. Last, participants with large RewP and high FMT were not associated with any of these particular traits.

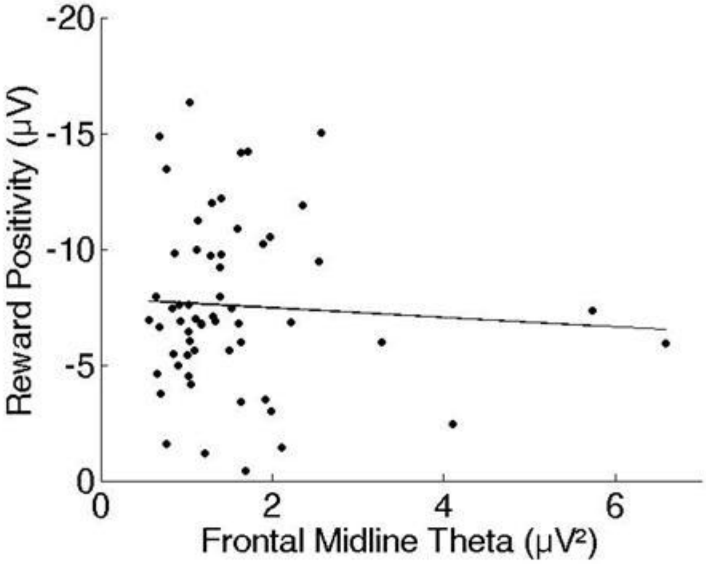


Figure 15. Scatterplot between reward positivity (RewP) (y-axis) and frontal midline theta (FMT) (x-axis) showing no correlation (see text). Negative is plotted up to align with the RewP waveforms.

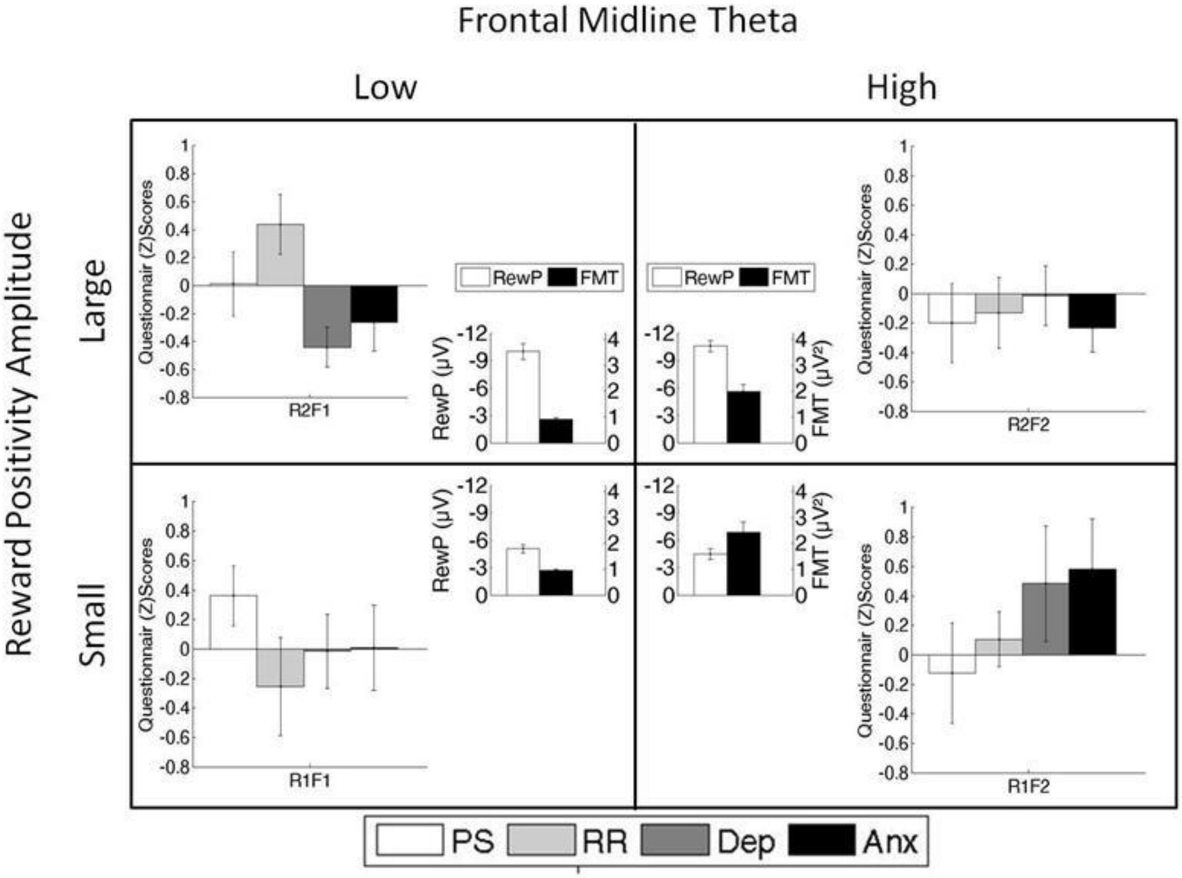


Figure 16. Exploratory analysis of the relation among reward positivity (RewP) amplitude, frontal midline theta (FMT), and four personality questionnaires; persistence scale (PS), reward responsiveness scale (RR), depression (Dep) and anxiery (Anx) subcomponent of the depression anxiety stress scale (DASS-21). RewP and FMT were separately median-splitted, and the combination was organized into quadrants, as shown in the middle of the quadrants (RewP is shown in white bars (on the left y-axis), while FMT is shown in black bars (on the right y-axis)). The upper left quadrant consists of participants with large RewP and low FMT. The lower left quadrant consists of participants with small RewP and low FMT. The upper right quadrant consists of participants with large RewP and high FMT. The lower right quadrant consists of participants with small RewP and high FMT. The size of each

personality traits (z-scored) are shown in a bar graph in each quadrant. Error bars indicate standard errors of the means.

What predicts depression scores?

To further characterize the profile of participants who showed elevated depression scores, a multiple linear regression was performed on the depression scores based on the personality traits (excluding the DASS-21 anxiety subscale, which is related to the depression subscale), RewP, and FMT. The analysis indicated that participants high in depression scores were characterized by low persistence, high FMT power, and smaller (more positive) RewP, F(3,53)=8.7, p<.01, explaining 33% of the variance (Figure 17) (see Table 6 for the detailed regression result).

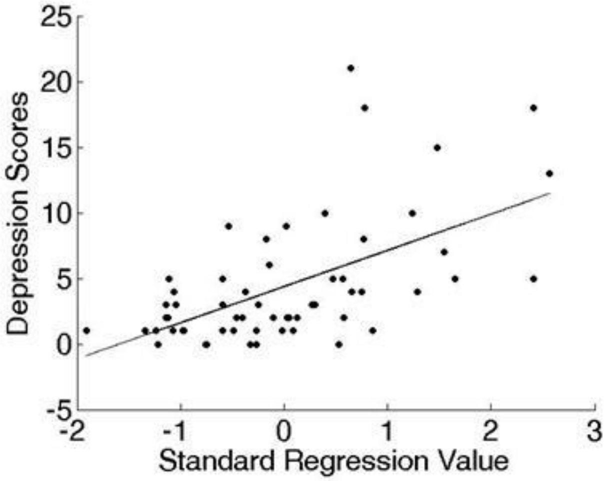


Figure 17. Results of a multiple regression analysis in which depression scores were predicted by the trait persistence, reward positivity (RewP), and frontal midline theta (FMT). These variables together (i.e., standardized predicted value on the x-axis) explain 33% of the variance in the depression scores (the y-axis).

Discussion

Participants performed a time estimation task for 2h, receiving a small monetary reward for each “on-time” estimate, the difficulty of which was adjusted across trials so that all of the participants received the rewards on approximately 50% of the trials. Furthermore, the participants were told that better performance increased the chance for receiving one of two $100 Amazon gift cards that were awarded to two of the participants. Interestingly, the effect of time on task on performance was statistically marginal, and TWS in fact continued to improve throughout the first 90 minutes (quarters 1-3), after which it fell somewhat during the final 30 minutes (quarter 4). As expected, RewP and P300 amplitudes both became smaller over time, suggesting that the reward value decreased and participants became less engaged in the task with time. By contrast, FMT power increased with time on task, which is suggestive of enhanced cognitive control needed to stay on task despite increasing levels of fatigue (see also Barwick et al., 2012; Boksem et al., 2005; Wascher et al., 2014). Larger (worse) TWS also correlated with smaller RewP and P300 amplitudes. The TWS-P300 correlation remained when RewP amplitude was controlled for, indicating that participants with smaller (better) TWS were likely to have been more attentive to the task. In addition, higher levels of task engagement as measured by a paper and pencil post-experiment self-reports correlated significantly with smaller (better) TWS, as well as with higher reward responsiveness and persistence scores, and somewhat reduced apathy scores. FMT did not correlate with TWS, RewP, or P300.

Although not all the effects reached statistical significance, some interesting statistical trends emerged when the above results were examined in relation to personality traits. First, participants high in depression scores and anticipatory pleasure performed worse overall. Although it is not clear exactly why increased anticipatory pleasure predicted worse performance, it may be that a mere anticipation of rewards is not sufficient to sustain prolonged task performance particularly when a task is as simple as estimating one second (but see Sherdell, Waugh, & Gotlib, 2012). Moreover, as noted elsewhere, TEPS is a relatively newly developed anhedonia scale whose psychometric properties are still being refined. Second, participants high in reward responsiveness and low in persistence produced larger RewPs. The association between high reward responsiveness and increased RewP is consistent with Experiment 1 and with previous reports (Bress & Hajcak, 2013), highlighting that RewP indexes reward sensitivity. Further, the finding of reduced (more positive) RewP in participants high in persistence is interesting: as the primary characteristic of trait persistence is to stay on task, particularly in the face of high task demands, it is likely that the rewards were less important for motivating these individuals to complete the experiment successfully. By contrast, participants high in reward responsiveness may place relatively more importance in each reward, thereby helping them to continue to perform the task. The finding that these participants also produced less FMT in the 2nd half compared to the 1st half of the experiment also aligns with the suggestion that their performance is sustained by the accumulation of small rewards, which is sufficient to sustain cognitive control over the long term, as indicated by the change in FMT.

On the other hand, participants high in cosummatory pleasure showed increased FMT in the 2nd half compared to the 1st half of the experiment. One might expect that high consummatory pleasure scores should be correlated with reduced FMT over time as this is also a measure of reward sensitivity as in reward responsiveness, above. However, this sub-component of the anhedonia scale (i.e., TEPS) is developed to measure pure hedonic capacity that is unrelated to anticipatory or motivational aspects of reward processing. In fact, as the Table 5 indicates, TEPS-C was not correlated with any other personality traits, while other reward sensitivity measures (i.e., reward responsiveness and TEPS-A) correlate with motivational traits (i.e., persistence and reduced apathy). It may be that participants high in pure hedonic capacity necessitate some mechanisms to stay on task as fatigue increases with time, one of which may be to increase control as seen in the larger FMT in the last half of the experiment. However, more investigation is needed to understand what aspect of consummatory pleasure TEPS actually assesses, as TEPS is a relatively newer anhedonia scale and its internal consistency is lower (e.g., Cooper et al., 2014; Liu et al., 2014) than the other scales used in this study.

Previous reports also found a strong association between FMT and anxiety (Mitchell et al., 2008; Cavanagh & Shackman, 2015). However, I only found a trend for increased anxiety scores with increased FMT when the size of RewP and FMT were examined by median-split. It may be that the anxiety-FMT link would be statistically stronger if FMT were analyzed trial-by-trial in response to each feedback stimulus, instead of the 4-second epochs utilized here, because an adaptive trial-by-trial behavioral adjustment in response to ambiguous or negative events appears to be moderated by anxiety (Cavanagh & Shackman, 2015). Alternatively, the anxiety questionnaire used in the present study (i.e., DASS-21) may not have accurately assessed anxiety as a personality trait, as this scale is more sensitive to state anxiety. Finally, the possibility that FMT contribute to co-morbid depression and anxiety symptoms would be an interesting avenue for future investigation. The occurrence of these two disorders is extremely high, and depression scores in the current study were associated with increased FMT, which I actually expected to be associated with the trait anxiety.

A primary question driving this study was whether high depression symptoms were associated with reduced task maintenance by ACC, which the HRL-ACC theory holds is responsible for sustaining extended behaviors (Holroyd & McClure, 2015; Holroyd & Yeung, 2012). This question was examined by regressing depression scores by the personality traits related to ACC function (i.e., persistence, reward responsiveness, TEPS, and apathy) and the two neural signatures of ACC, RewP and FMT. The result indicated that reduced persistence, reduced RewP amplitude and increased FMT power predicted high depression scores. Anhedonia is often thought to be the defining characteristic of depression, but this finding that low persistence predicted high depression scores supports the hypothesis that task maintenance may also be reduced in individuals high in depression scores. Interestingly, reduced RewP predicted high depression scores beyond any of the reward-related traits, corroborating the hypothesis that RewP can serve as a biomarker for depression (Proudfit, 2015). Moreover, higher FMT predicting higher depression scores is also intriguing. In depressed individuals, hypoactivity in brain areas responsible for cognitive control has often been observed (e.g., DLPFC and dACC) (see Pizzagalli, 2011), as well as reduced willingness to exert effortful behavior (as discussed in Experiment 3 and elsewhere; see Treadway et al., 2009; Treadway & Zald, 2011). Taken at face value, the relatively higher FMT may indicate that individuals high in depression scores may have found the task to be more cognitively fatiguing. Supporting this idea, a recent study found that depressed patients exerted relatively less effort than control subjects did when working to obtain large rewards, yet their subjective reports of perceived effort to obtain those rewards was as high as that of the control subjects, pointing to a discrepancy between subjective and objective indicators of effort (Cléry-Melin, Schmidt, Lafargue, Baup, Fossati, &

Pessiglione, 2011). Similarly, lateral PFC and dACC were more activated in a working memory task for depressed individuals compared to healthy individuals in an fMRI experiment, which was interpreted as a compensatory response by these regions in order for patients to perform the task at a similar performance level to their healthy counterparts (Harvey et al., 2005). Therefore, participants high in depression scores in the current study may have found the task particularly fatiguing, despite subjective perceptions of high effort, leading to worse task performance. Nevertheless, this finding warrants further investigation and replication.

Despite these observations it bears repeating that several of these findings related to personality differences exhibited only statistical trends ($p<.1$). More research is therefore needed to further understand the neural mechanisms underlying extended behavior. For instance, the time-estimation task that I employed here reliably measures RewP and FMT (and their associated cognitive control processes) but does not have an affective component. Future investigations could examine the effect of emotional states and/or task difficulty on extended behavior. Also, the relation between the high relapse rates in depression and extended behaviors would be important to study, as individual differences in extended, goal-directed behaviors may predict individuals' vulnerability to relapse. In this context, it is interesting to note that both high persistence and high depression scores were associated with reduced RewP, yet what appeared to distinguish between these traits was the difference in participant ability to sustain prolonged behavior. For instance, larger (worse) TWS was associated with higher depression scores but not with persistence scores, which were instead correlated with enhanced self-reports of task engagement. Much of our daily life consists of actions that progress towards a distal goal, which requires us to maintain extended, goal-directed behaviors even in the absence of immediate rewards and despite various challenges along the way. Therefore, to achieve a distal goal, adequate reward sensitivity *and* the ability to persist even in the absence of immediate reward are both essential traits. Persistent individuals appear to lack the former but possess the latter, which manifests when they are faced with challenges, namely when they need to persist to achieve a long term goal (like completing a PhD thesis) with few rewards along the way. By contrast, neither trait would appear to be strong in individuals high in depression scores, indicating that it would be particularly hard for these individuals to progress towards a long term goal. Future investigations may also focus on early indications that are predictive of poor performance on extended tasks as for instance, it is difficult to engage clinical patients in tasks for prolonged periods of time.

Experiment 3

Experiment 3 extended Experiment 2 by investigating sustained performance of tasks that demand physical effort, which appear to recruit ACC more strongly. An extensive literature based on animal studies implicates dACC (Walton, Bannerman, & Rushworth, 2002; Floresco & Ghods-Sharifi, 2007; Rudebeck, Walton, Smyth, Bannerman, & Rushworth, 2006; Walton et al., 2009) and the striatum, including the nucleus accumbens (Salamone, Correa, Mingote, & Weber, 2003) in effortful behavior. dACC lesions cause non-human animals to “slack off” by shifting their preference away from high-effort, high reward choices to low-effort, low-reward choices (Floresco & Ghods-Sharifi 2007; Hosking, Cocker, & Winstanley, 2014; Kennerley, Dahmubed, Lara, & Wallis, 2009; Walton et al. 2002, 2009). In humans, the lesion leads to apathy (Eslinger and Damasio, 1985; van Reekum et al., 2005). Integration of reward and effort-related information likely occurs via interactions with the midbrain DA system, as DA depletion and DA antagonists reduce effortful behaviors (Phillips, Walton, & Jhou, 2007; Salamone & Correa, 2002; Salamone, Steinpreis, McCullough, Smith, Grebel, & Mahan, 1991; Salamone, Correa, Farrar, Nunes, & Pardo, 2009 for review), while DA agonists (such as amphetamine) increase effortful behaviors (Bardgett, Depenbrock, Downs, Points, & Green, 2009; Floresco, Maric, & Ghods-Sharifi, 2008), indicating DA’s role in overcoming effortful costs. Studies in humans parallel this research in non-human animals (Croxson et al., 2009; Kurniawan et at., 2010; Prévost et al., 2010). For example, individual differences in DA release predict willingness to expend greater effort for larger rewards, and amphetamine administration increases effortful behavior, particularly when the probability for receiving reward is low (Treadway et al., 2012b; Wardle et al., 2011).

Although both dACC and striatum are implicated in the production of effortful behaviors, dACC appears to be involved particularly in effortful behavior sustained over time. For instance, dACC exhibits a sustained increase in activity during continued effortful performance directed toward obtaining rewards, both in non-human animal (Blanchard et al., 2015; see also Kennerley et al., 2006) and human (Croxson et al., 2009) subjects. Moreover, sustained dACC activity appears to be associated with the personality trait of persistence (Cloninger et al., 1993), which is characterized by the tendency to exert self-regulatory control, a trait that is lacking in individuals who are apathetic (see introduction. Blanchard et al., 2015; Parvizi et al., 2013). For instance, increased dACC activity was observed when human participants high in the personality trait persistence rejected low-effortful choices in favor of more effortful choices in an fMRI study (Kurniawan et al., 2010).

Recent studies suggest that depression, particularly when occurring with anhedonia, is associated with a reduced willingness to expend effort to obtain rewards (Clery-Melin et al., 2011; Sherdell et al., 2012; Treadway et al., 2009). These observations were interpreted to mean that anhedonia is not merely a deficit of “liking” reward but rather one of “wanting” reward, such that anticipating rewards and translating incentive motivation into subsequent actions may be impaired in individuals with depression. Here I extended these findings by having participants engage in an effortful task for a prolonged period of time (i.e., 1 hour) while their brainwaves were recorded. On each trial participants were asked to choose between performing an easy behavior (i.e., a low-force squeeze on a hand-dynamometer) and a hard behavior (a high-force squeeze on the hand-dynamometer) to obtain smaller or larger rewards, respectively, and then to carry out that behavior. Response choice (i.e., low vs. high effort), RewP, and FMT were examined in relation to personality traits. I predicted that participants characterized by high persistence would exhibit greater degrees of effortful behavior, particularly when the probability of reward receipt was low, whereas participants characterized by low motivation and low reward sensitivity (e.g., as observed in individuals high in apathy, anhedonia, and depression scores) would show a bias toward the selection of low-effort, easy choices. Furthermore, I predicted that individuals who scored high in depression would exhibit relatively less effortful behavior with time on task, consistent with the expectation that they would have difficulty continuing to perform high-effort actions for a sustained period of time.

Materials and methods

Participants

Seventy-seven undergraduate students were recruited from the University of Victoria Department of Psychology subject pool to fulfill a course requirement or earn bonus credits. All subjects (26 males, 8 left-handed, age range=18-35 years, mean age =21.5 +/- 3.8 years) had normal or corrected-to-normal vision. Each participant also received a monetary bonus in addition to the credits, the amount of which depended on their task performance (see below). All subjects provided informed consent as approved by the local research ethics committee. The experiment was conducted in accordance with the ethical standards prescribed in the 1964 Declaration of Helsinki.

Grip force calibration

Physical effort expenditure was measured using a hand-dynamometer (Neulog, U.S.). Each participant's maximum grip strength was measured before the experiment began. The hand-dynamometer was affixed to the table in a straight-up position in front of the computer screen (approximately 36 cm from the participants and 18 cm from the computer screen). Participants exerted their maximum grip force for 2 seconds, 5 times for both their right hand and left hand. The largest force produced by each hand was then taken as the maximum grip force for that hand throughout the experiment.

Task Design

I modified the Effort-Expenditure for Rewards Task (Treadway et al., 2009) such that subjects responded by squeezing the hand-dynamometer (instead of executing a rapid series of button presses, as in the original study) to adapt it for an EEG experiment.

First, during an initial Practice Phase, on each trial participants selected between two choices described as “Easy” and “Hard” in large font on either side of the center of the computer screen (Figure 18a, 1st panel from left), by pressing a corresponding right or left arrow key. The selected choice was then highlighted by a red frame (1 s) (Figure 18a, 2nd panel from left), followed by a “Ready” screen (1 s) (Figure 18a, 3rd panel from left), which indicated to participants that they should prepare to squeeze the device. Next, an image appeared of a white rectangular bar bisected with a red horizontal line, indicating that they should squeeze the hand-dynamometer. The height of the white rectangular bar was adjusted to the maximum grip force for the responding hand of that participant, with the half-way point located at the center of the screen. The red horizontal line indicated the minimum grip force required to achieve a successful squeeze response for that trial.

Crucially, on each trial the red threshold was set 40% +/- 5% and 85% +/- 5% of the participant's maximum squeeze force for the low-effort behavior ("easy choice") and high-effort behavior ("hard choice"), respectively. Further, as subjects squeezed the dynamometer, the base of the white bar was replaced with the color black, the height of which was proportional to the applied force, providing visual feedback to the subject on the strength of their response (Figure 18a, 4th panel from left). Participants were given 2 s maximum for their response to exceed the threshold, after which the image was replaced with a fixation dot at the center of the screen (1 s) (Figure 18a, 5th panel from left). If the applied force exceeded the response threshold, then the words "Good job!" appeared at the center of the screen, otherwise the words "Squeeze harder" were presented (1 sec) (Figure 18a, 6th panel from left). Finally, the instructions "Release Grip" appeared at the center of the screen (500 ms) to ensure that the participants relaxed their grip before starting the following trial (Figure 18a, last panel from left). The location of the effort choices (left or right side of the screen) and the mappings between the choice and the response finger were counterbalanced across participants but were maintained throughout the experiment for each participant. Participants practiced executing the easy and hard choices once each for each hand, for a total of four trials.

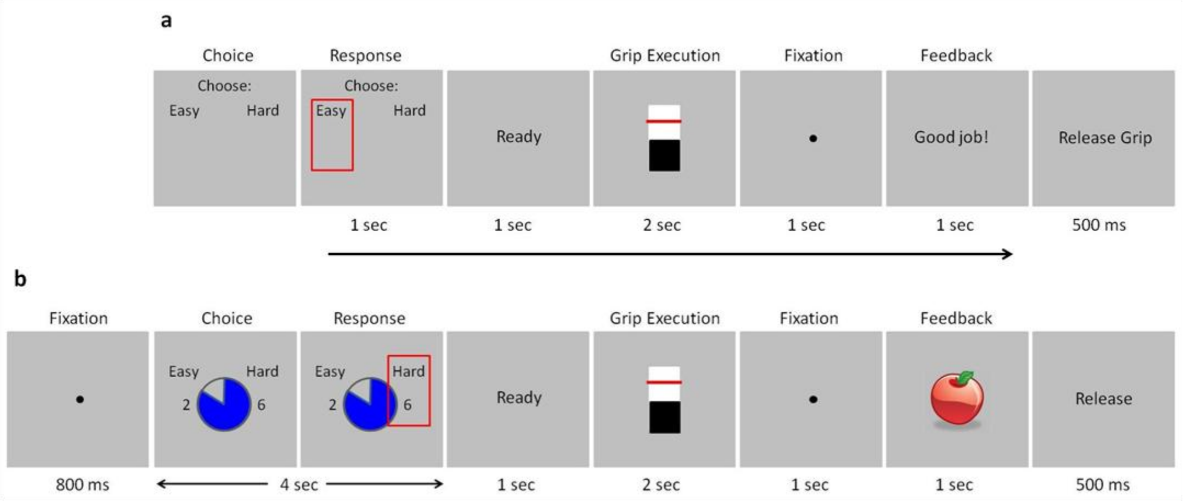


Figure 18. An example sequence of one trial during the initial Practice Phase (a) and during the actual experiment (b) in Experiment 3.

After participants were familiarized with the level of effort required to respond to the easy and hard choices for both hands, they were then presented with several practice trials in which their choices incorporated information about reward and reward probability. Now, on each trial an image of a pie chart was presented at the center of the choice screen (Figure 18b, 2nd panel from left). Participants were instructed that successful responses to the easy choice would always yield a chance to earn a 2 cents reward, whereas successful responses to the hard choice would yield a chance to earn between 3 and 8 cents reward, determined at random (as selected from a normal distribution function). Unsuccessful responses always resulted in 0 cents reward. The probability of obtaining the reward was low (20%), medium (50%) or high (80%) (pseudo-randomly determined, see below) regardless of the choice made (i.e., the probability for reward was the same irrespective of whether the easy or hard choices was selected). Participants selected a choice and then responded as above; immediately following completion of their squeeze response a fixation stimulus appeared at the center of the screen (1 sec), followed by a feedback stimulus consisting of either of two fruit images (1 sec) (Figure 18b, 7th panel from left). For half the participants an image of an apple and an image of an orange indicated that they either won or did not win, respectively, the money for the selected choice on that trial; the mapping between feedback stimuli and reward valence was reversed for the other half of the participants. Participants were given six practice trials (three trials with each hand) involving reward probability and amount. Participants were given their accumulated reward upon completion of the practice phase (between 5 and 25 cents).

Last, subjects began the task proper (Figure 18b), which was identical to the Practice Phase except that 1) each trial began with a fixation dot presented at the center of the screen (800ms; Figure 18b, 1st panel from left), 2) the word “Choose:” and the cents sign “₵” did not appear during the choice panel, and 3) the choice deadline was extended to 4s (Figure 18b, 2nd & 3rd panels from left). When a choice between effort levels was made within the 4 s deadline, then the choice was highlighted with a red frame for the remainder of the 4 s (e.g., if the response was completed after 3 seconds following the onset of the choice screen, then the red frame appeared for the remaining 1 sec). If an effort choice was not made during the 4s period, then a “Respond faster” message appeared (500 ms) and the same trial was repeated.

Procedure

Participants were tested in the same experimental environment as described in Experiments 1 and 2. A brief set of instructions presented on the computer screen described the task, indicating that they would be using a hand-dynamometer in order to have a chance to win monetary rewards. This was followed by the procedure for calibrating each participant’s hand-grip strength (see above). Following the task practice outlined above, the actual experiment began. Participants completed eight blocks of 39 trials each, which lasted approximately 1 hour. In order to ensure a sufficient number of trials for the ERP analysis for the 50% reward probability condition, the reward probability on each trial was chosen pseudo-randomly so that trials with 50% reward probability occurred about twice as often (25 trials per block) as the 20% and 80% reward probability trials combined (7 trials each per block). Each block lasted about 7 minutes with self-paced between-block rest periods. Participants were told simply that the goal of the study was to perform the task as best as they could. At the beginning of each block of trials a screen indicated which hand they should use for the upcoming block of trials (randomly determined for each participant), which alternated on each block in order to minimize muscle fatigue. After completing each block of trials the participants were queried on the computer screen about the correct mapping between the fruit images and reward feedback stimuli (i.e., “Press the 1 key if apple is reward and press the 2 key if orange is reward”), in order to ensure that they remembered the designated valences of the feedback stimuli. The sum total of their accumulated earnings for that block was also presented. When participants completed the task they were shown the total amount of reward they had earned, which ranged between $4 and $8.8. At the end of the experiment each participant’s hand-grip strength was re-calibrated three times for each hand. At this point the participants answered six personality questionnaires (see below).

Questionnaires

The same six personality questionnaires as in Experiment 2 were administered.

Data Analysis

Behavior

Effort bias (i.e., the likelihood of choosing the harder (high-effort) choice over the easier (low-effort) choice) was calculated as (H-E)/(H+E), where H denotes the number of trials the hard choice was selected and E denotes the number of trials the easy choice was selected; larger ratios indicate greater preference for the harder choice. To examine changes in the effort bias over time, the ratio was also calculated between the 1st half and 2nd half of the experiment by subtracting the effort bias ratio in the 1st half of the experiment (i.e., approximately the first 30 min) from the effort bias ratio in the 2nd half of the experiment (i.e., approximately the last 30 min). Here larger ratios indicate greater preference for the harder choice in the 2nd compared to the 1st half of the experiment.

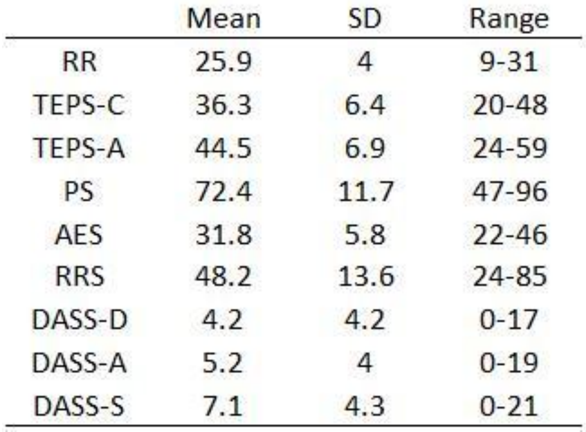
Electrophysiology

Data acquisition and pre-processing (for both the ERP and FFT analyses) were identical to those in Experiment 2 except that the data were filtered offline with a passband of 0.10–20 Hz as in Experiment 1. RewP amplitude was measured as in Experiment 2, except that the window for identifying the ERP component extended from 200 to 300 ms post-feedback, as determined by visual inspection of each participant's ERP waveforms. Following the procedure in Experiment 2 a FFT analysis was conducted to examine FMT during the choice period. The EEG data were segmented into 4 s epochs corresponding to the entire duration of the choice period. FMT was assessed by averaging power between 4 and 8 Hz at channel FCz, where FMT is typically greatest and where it was maximal in the present study. The difference in FMT between the easy and the hard choice was calculated as a ratio by subtracting average FMT on trials in which the easy choice was selected from average FMT on trials in which the hard choice was selected, and dividing this quantity by the total sum of these two quantities. Note that larger ratios indicate greater FMT in the hard choice relative to the easy choice.

All of the analyses were conducted in SPSS (IBM SPSS 23). Multiple linear regression analyses were performed using the same method as in Experiment 1 and 2. Only statistically significant models are reported. The EEG analyses included only trials from the 50% reward probability condition as the other probability conditions did not contain sufficient numbers of trials for this purpose. Furthermore, as the effort choice on each trial was voluntary, for some participants some conditions did not have enough trials for the electrophysiological analyses. For instance, a few participants selected the hard choice on a majority of trials, yielding an insufficient number of trials for creating ERP averages to the easy choice. Only data for participants with at least 20 trials in each choice condition were included for each analysis. Note that the number of participants included for each analysis is indicated in the degrees of freedom for each statistical test. Finally, the influence of outliers was treated according to the jackknife procedure discussed in the introduction.

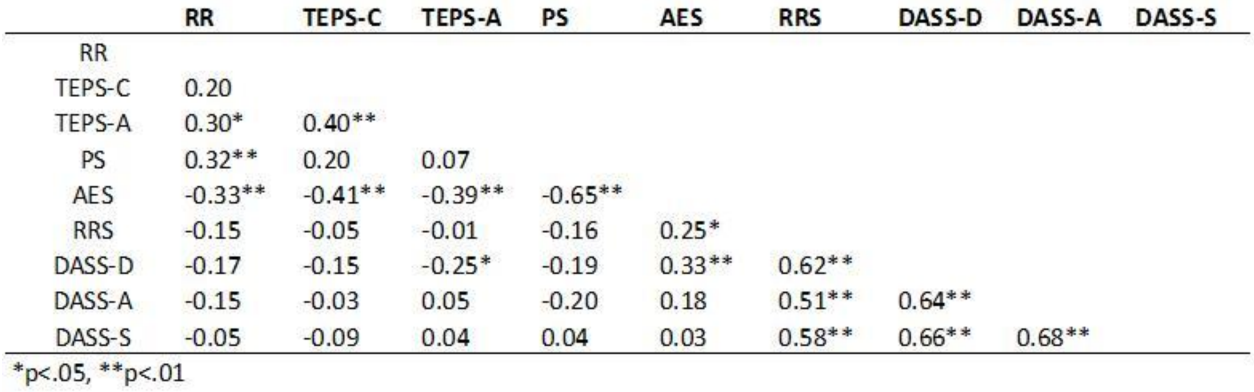
Results

The data of seven participants were excluded from the analyses. One participant discontinued the experiment due to feeling unwell, two participants did not understand the task instructions due to difficulty with English comprehension, three participants' data were excluded due to a programming error, and the performance of one participant was extremely low (a 62% success rate averaged across easy and hard choices and 24% success rate for the hard choice). Therefore, results from a total of 70 participants are reported here. A summary of questionnaire scores are provided in Table 7, and zero-order correlations among the questionnaire scores are provided in Table 8.



	Mean	SD	Range
RR	25.9	4	9-31
TEPS-C	36.3	6.4	20-48
TEPS-A	44.5	6.9	24-59
PS	72.4	11.7	47-96
AES	31.8	5.8	22-46
RRS	48.2	13.6	24-85
DASS-D	4.2	4.2	0-17
DASS-A	5.2	4	0-19
DASS-S	7.1	4.3	0-21

Table 7. A summary of participant questionnaire scores in Experiment 3. For abbreviations see Table 1 and Table 4.



	RR	TEPS-C	TEPS-A	PS	AES	RRS	DASS-D	DASS-A	DASS-S
RR									
TEPS-C	0.20								
TEPS-A	0.30*	0.40**							
PS	0.32**	0.20	0.07						
AES	-0.33**	-0.41**	-0.39**	-0.65**					
RRS	-0.15	-0.05	-0.01	-0.16	0.25*				
DASS-D	-0.17	-0.15	-0.25*	-0.19	0.33**	0.62**			
DASS-A	-0.15	-0.03	0.05	-0.20	0.18	0.51**	0.64**		
DASS-S	-0.05	-0.09	0.04	0.04	0.03	0.58**	0.66**	0.68**	

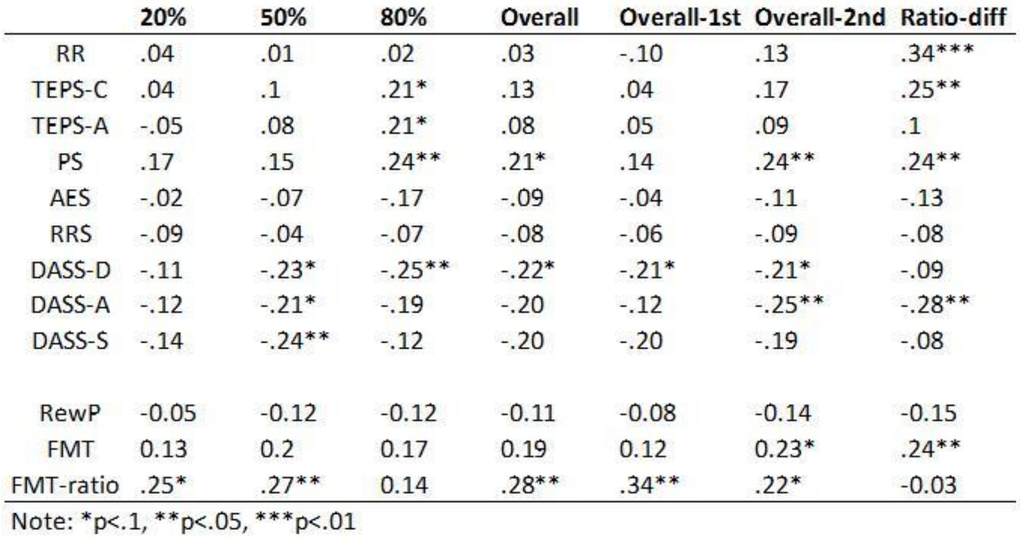
*p<.05, **p<.01

Table 8. Zero-order correlations among questionnaire scores.

Behavior

The average success rate across both choices (97% +/- 4%) was not significantly correlated with individual personality questionnaire scores (all p>.1), but was positively correlated with the effort bias (r=.38, p<.01) – the likelihood of choosing the hard choice over the easy choice (see methods) -- indicating that participants who selected the hard choice more often than the easy choice tended to be more successful at completing their choices. A repeated measures ANOVA on the effort bias with reward probability as a within-subject factor (20%, 50%, or 80%) revealed a significant effect of probability, F(1.6,107)=171, p<.01, η_p^2= .71 (Greenhouse-Geisser corrected). Further, post-hoc analysis revealed a linear trend such that effort bias was largest in the 80% reward probability condition (.64 +/- .44), second largest in the 50% condition (.24 +/- .52), and smallest in the 20% condition (-.39 +/- .56), F(1,69)=222, p<.01, η_p^2=.76. In other words, participants tended to choose the hard choice more often when the reward probability was high.

Table 9 provides a summary of zero-order correlations between the effort bias and personality questionnaires. Consistent with the previous finding (Treadway et al., 2009) participants high in depression scores were relatively less likely than other individuals to make effortful choices, especially when the reward probability was high. By contrast, participants high in persistence were more likely to exert effort, especially during the latter half compared to the first half of the experiment.



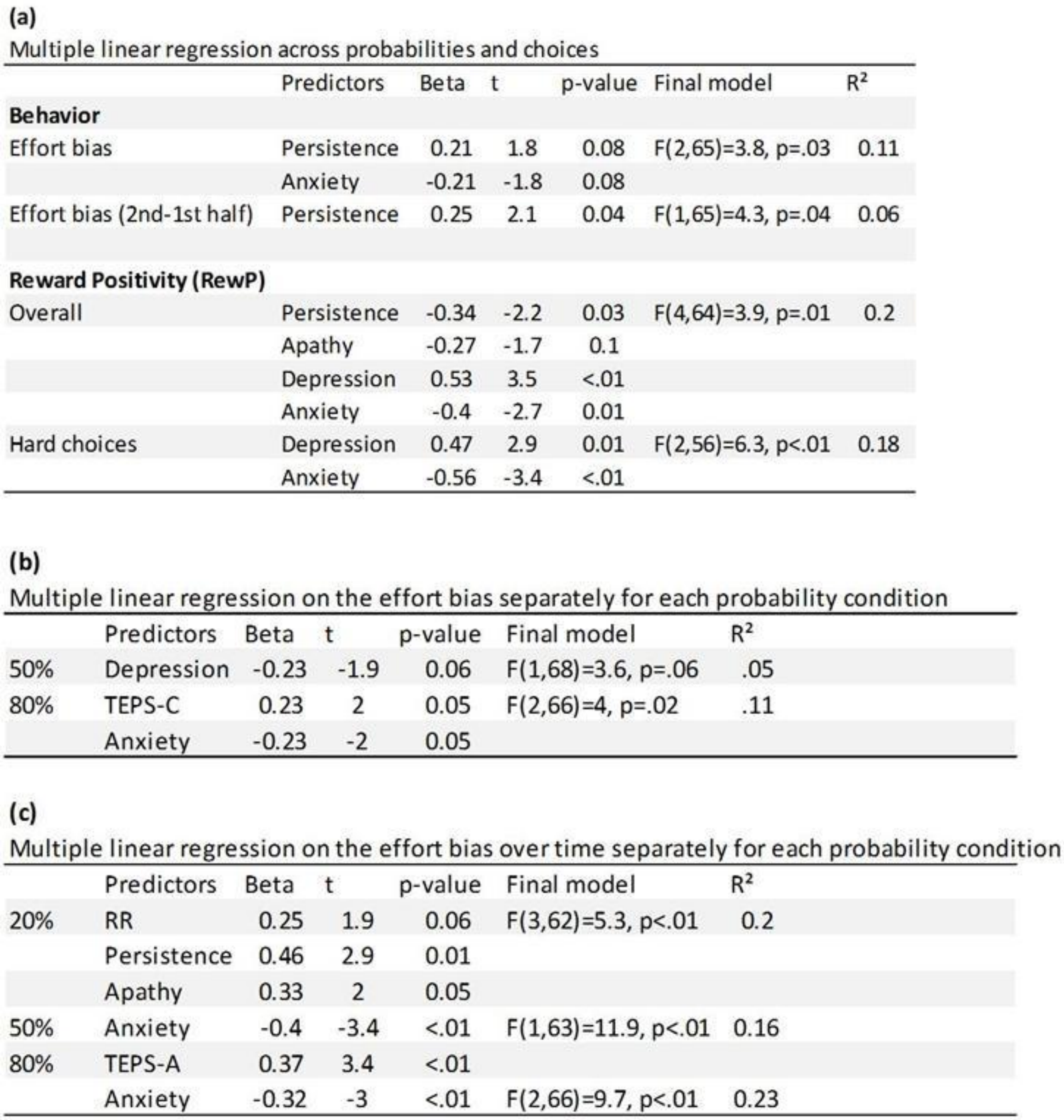
	20%	50%	80%	Overall	Overall-1st	Overall-2nd	Ratio-diff
RR	.04	.01	.02	.03	-.10	.13	.34***
TEPS-C	.04	.1	.21*	.13	.04	.17	.25**
TEPS-A	-.05	.08	.21*	.08	.05	.09	.1
PS	.17	.15	.24**	.21*	.14	.24**	.24**
AES	-.02	-.07	-.17	-.09	-.04	-.11	-.13
RRS	-.09	-.04	-.07	-.08	-.06	-.09	-.08
DASS-D	-.11	-.23*	-.25**	-.22*	-.21*	-.21*	-.09
DASS-A	-.12	-.21*	-.19	-.20	-.12	-.25**	-.28**
DASS-S	-.14	-.24**	-.12	-.20	-.20	-.19	-.08
RewP	-0.05	-0.12	-0.12	-0.11	-0.08	-0.14	-0.15
FMT	0.13	0.2	0.17	0.19	0.12	0.23*	.24**
FMT-ratio	.25*	.27**	0.14	.28**	.34**	.22*	-0.03

Note: *p<.1, **p<.05, ***p<.01

Table 9. A summary of zero-order correlations between effort bias and personality questionnaires, reward positivity (RewP), and frontal midline theta (FMT). FMT ratio = the ratio comparing the amount of FMT during the hard choice trials with FMT during the easy choice trials (see text). Overall = the effort bias collapsed across probabilities. Overall-1st = same as the Overall but during the 1st half of the experiment. Overall-2nd = same as the Overall but during the 2nd half of the experiment. Ratio-diff = the difference in the effort bias between the 2nd half and 1st half of the experiment (see text).

A multiple linear regression analysis on the effort bias averaged across all the probabilities, with the individual questionnaire scores serving as predictors, revealed that participants high in anxiety scores and low in persistence were more likely to select the easy choice, F(2,65)=3.8, p=.03, explaining 11% of the variance (Table 10a). Multiple regression analyses conducted separately for each probability condition indicated that participants high in depression and anxiety scores and low in consummatory pleasure produced fewer effortful behaviors when reward probability was at or above 50% (Table 10b).

Changes in the effort bias between the 1st half and 2nd half of the experiment were also examined in a multiple linear regression analysis. The analysis indicated that participants high in persistence exhibited an increased effort bias in the 2nd half compared to the 1st half of the experiment, F(1,65)=4.3, p=.04, explaining 6% of the variance (Table 10a). Consistent with the zero-order correlations indicating a significant positive correlation between persistence and the effort bias in the 2nd half of the experiment (“Overall-2nd” in Table 9) but not in the 1st half of the experiment (“Overall-1st” in Table 9), the regression result indicates that individuals high in persistence selected the hard choice more often than the easy choice in the 2nd half of the experiment, relative to the choice behavior of other participants. Multiple regression analyses conducted separately for each probability condition indicated that participants high in motivational traits (i.e., persistence, reward responsiveness, and anticipatory pleasure (TEPS-A)) showed increased effort bias with time on task (i.e., in the 2nd half compared to the 1st half of the experiment) while participants high in anxiety scores showed reduced effort bias with time on task (Table 10c). However, a puzzling finding is that participants high in apathy also exhibited a larger effort bias in the 2nd half of the experiment as compared to the 1st half of the experiment in the 20% reward probability condition, along with participants high in reward responsiveness and persistence. A possible reason for this is discussed in the discussion section, below.



(a)

Multiple linear regression across probabilities and choices

	Predictors	Beta	t	p-value	Final model	R²
Behavior						
Effort bias	Persistence	0.21	1.8	0.08	F(2,65)=3.8, p=.03	0.11
	Anxiety	-0.21	-1.8	0.08		
Effort bias (2nd-1st half)	Persistence	0.25	2.1	0.04	F(1,65)=4.3, p=.04	0.06
Reward Positivity (RewP)						
Overall	Persistence	-0.34	-2.2	0.03	F(4,64)=3.9, p=.01	0.2
	Apathy	-0.27	-1.7	0.1		
	Depression	0.53	3.5	<.01		
	Anxiety	-0.4	-2.7	0.01		
Hard choices	Depression	0.47	2.9	0.01	F(2,56)=6.3, p<.01	0.18
	Anxiety	-0.56	-3.4	<.01		

(b)

Multiple linear regression on the effort bias separately for each probability condition

	Predictors	Beta	t	p-value	Final model	R²
50%	Depression	-0.23	-1.9	0.06	F(1,68)=3.6, p=.06	.05
80%	TEPS-C	0.23	2	0.05	F(2,66)=4, p=.02	.11
	Anxiety	-0.23	-2	0.05		

(c)

Multiple linear regression on the effort bias over time separately for each probability condition

	Predictors	Beta	t	p-value	Final model	R²
20%	RR	0.25	1.9	0.06	F(3,62)=5.3, p<.01	0.2
	Persistence	0.46	2.9	0.01		
	Apathy	0.33	2	0.05		
50%	Anxiety	-0.4	-3.4	<.01	F(1,63)=11.9, p<.01	0.16
80%	TEPS-A	0.37	3.4	<.01		
	Anxiety	-0.32	-3	<.01	F(2,66)=9.7, p<.01	0.23

Table 10. A summary of the multiple regression results.

Electrophysiology

RewP was analyzed for the 50% reward probability condition as indicated above. RewP exhibited a frontal-central maximum as expected (Figure 19d), at channel FCz where it commonly reaches maximum amplitude; although RewP was numerically larger at channel Cz, the comparison between the two channels was non-significant (p>.5). As expected, a one-sample t-test revealed that RewP amplitude averaged across the effort choices (-3.9 μV +/-3.1 μV) was more negative than zero, t(69)=-10.6, p<.01 (Figure

19a). Likewise, RewP amplitude was significantly more negative than zero when averaged separately for the easy choice (-3.9 µV, +/-3.4 µV), t(42)=-7.5, p<.01, and for the hard choice (-4.2 µV +/-3.5 µV), t(58)=-9.1, p<.01 (Figure 19b & c). For the 32 participants who chose the two options about equally (providing enough trials to examine RewP amplitude for each condition), a paired t-test did not reveal a significant effect of choice difficulty on RewP amplitude (p>.8).

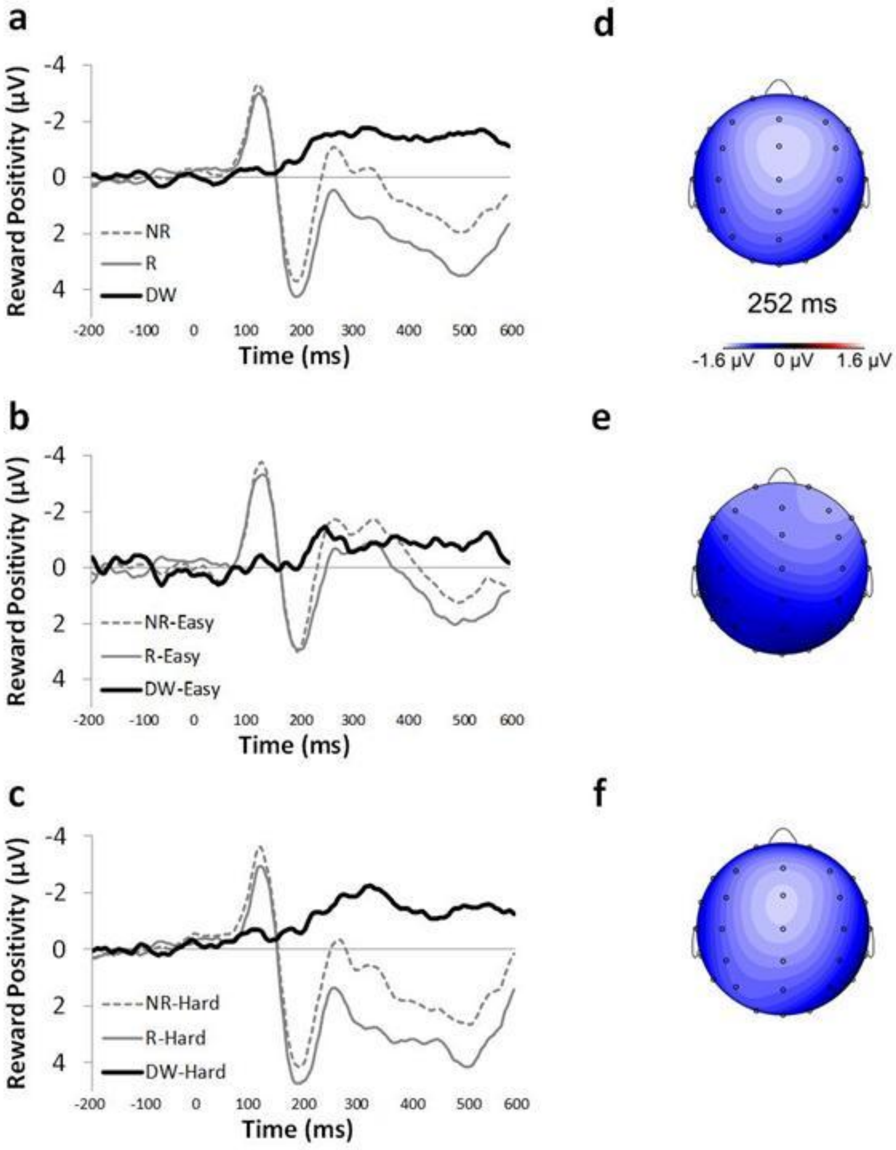


Figure 19. Event-related brain potentials (ERPs) elicited by reward (solid gray line) and no-reward (dashed gray line) feedback stimuli. The difference wave (i.e., RewP) is shown by the black line. (a) collapsing across both the easy and the hard choices, (b) for the easy

choice, and (c) for the hard choice. Associated scalp distributions are shown for (d) both the easy and hard choices collapsed, (e) for the easy choice, and (f) for the hard choice. The voltage on the y-axis is plotted negative up by convention. The x-axis shows time in ms.

RewP amplitude averaged across choices was not correlated with any of the behavioral measures shown in Table 9 (p>.1). A multiple regression analysis on RewP amplitude averaged across choices with individual questionnaire scores serving as predictors indicated that participants high in depression scores produced smaller (more positive) RewPs while participants high in persistence, apathy, and anxiety scores produced larger (more negative) RewPs, F(4,64)=3.9, p=.01, explaining 20% of variance (Table 10a). Depression and anxiety scores predicted RewP amplitude particularly following hard choice responses, as revealed by the same analysis performed for the hard choice (N=58): following the response on hard trials the RewP was smaller for participants high in depression scores and larger for participants high in anxiety scores, F(2,56)=6.3, p<.01, explaining 18% of variance. No significant model was found for the easy choice.

Zero-order correlations between the FMT ratio (reflecting the difference in FMT power between the hard and easy choices) and the effort bias indicated that relatively more FMT for hard choices relative to easy choices predicted a higher probability of selecting the hard choice over the easy choice (Table 9). FMT across choices was also correlated with the difference in the effort bias between the 2^{nd} half and 1^{st} half of the experiment. Specifically, Larger FMT indicated increased propensity to select the hard choice in the 2^{nd} half of the experiment compared to the 1^{st} half of the experiment. This effect appeared driven by the 2^{nd} half of the experiment as larger FMT was marginally correlated with the effort bias only in the 2^{nd} half (p=.06) but not in the 1^{st} half of the experiment (p=.33) (Table 9).

A multiple linear regression analysis on FMT and the FMT ratio with the individual questionnaire scores serving as predictors did not reveal any significant models.

Discussion

The present study extended Experiment 2 by examining extended behavior involving physical effort. Further, participants were allowed to freely make effort-related choices themselves. I expected that this task would recruit greater ACC activity as ACC appears to be more strongly involved for physically demanding tasks and voluntary task selection. Participants performed a task in which on each trial they were free to choose between executing either a high-effort or a low-effort behavior (a hard choice and an easy choice, respectively) by squeezing a hand-dynamometer. A successful hand squeeze response resulted in an opportunity to earn monetary rewards according to one of three reward probabilities (20%, 50%, or 80% reward probability). The potential reward was always 2 cents for the easy choice, while the reward size varied randomly between 3 and 8 cents for the hard choice. Unsuccessful responses always resulted in no-reward. Participants performed the task for about an hour while their brainwaves were recorded, and the accumulated reward was given to participants at the completion of the task. Participants also completed a total of six personality questionnaires, and the task performance and ERPs were examined in relation to individual differences in personality traits.

Participants' effort choices were influenced by the reward probability such that the hard choice was selected more often than the easy choice (i.e., the effort bias was higher) when the reward probability was high (50% or above). Across probabilities, participants who scored high in persistence and low in anxiety selected the hard choice more often than the easy choice. This effect of persistence on a physically demanding task corroborates a previous fMRI study finding of increased dACC activation where participants high in persistence rejected easy choices (Kurniawan et al., 2010). The same analysis conducted separately for each reward probability condition indicated that participants high in depression or anxiety scores exhibited a smaller effort bias whereas participants high in consummatory pleasure exhibited a larger effort bias for high reward probabilities (50% or above). This result is also consistent with the previous reports that both healthy participants high in anhedonia and patients with depression produced fewer effortful behaviors, particularly for high reward probabilities (Treadway et al., 2009; see also, Treadway et al., 2012). As the investigators of that study noted, conditions with high reward probabilities might be expected to elicit increased effort expenditure; yet, as I will discuss later, the finding above is consistent with the results of Experiment 1, wherein participants high in depression scores produced smaller RewPs, especially when the rewards were probable. Also, unlike the participants high in depression scores, the participants who exhibited low anhedonia scores – that is, who scored high in both consummatory and anticipatory pleasure -- expended relatively more effort to obtain highly probable rewards (i.e., when offered a choice with an 80% reward probability). By contrast, an interesting effect of anxiety scores on the effort bias was unexpected, particularly in light of task performance over time, as discussed next.

Participants high in persistence selected the effortful choice more often in the last half of the experiment (i.e., the last 30 min) compared to the 1st half of the experiment (the first 30 min). These participants appeared specifically to exert more effort in the last half of the experiment relative to other individuals, as simple correlation analyses indicated a significant positive correlation between persistence and effort bias only during the 2nd half of the experiment, and not during the 1st half of the experiment. The same analysis conducted separately for each reward probability condition indicated that participants high in traits related to motivation (persistence, reward responsiveness, and anticipatory pleasure) selected the effortful choice more often in the last half of the experiment. However, unexpectedly, the regression analysis also indicated a relation between high apathy scores and increased effort with time on task for improbable rewards. This finding did not appear to be due to differences in the effort bias in the 1st half of the experiment (i.e., during the first half of the experiment, participants high in apathy selected both choices with similar frequency to those low in apathy). One possible explanation relates to an unexpectedly high correlation between apathy and persistence. Another possibility is that apathy subtypes may relate differently to effortful control. The apathy scale used in this study consisted of cognitive, emotional, and behavioral apathy (Marin et al., 1991), and a recent fMRI study indicated a strong association between behavioral apathy, which is characterized by a lack of self-initiated actions, and dACC activity (Bonnelle et al., 2015). Hence, more research is needed to clarify the relationship between apathy and effort bias over time, so these results should be interpreted with caution.

Interestingly, the more anxious participants selected the effortful choice less often in the last half compared to the first half of the experiment, particularly when the reward probabilities were high (at or above 50%). At first glance one might expect a similar result for the participants who scored high in depression. Yet, these participants selected fewer effortful choices from early on, as seen in a smaller effort bias already in the first half of the experiment (Table 9, under "Overall-1st" and "Overall-2nd"), whereas anxious participants selected the effortful choice less later in the experiment, as indicated by a significant negative correlation with anxiety scores only in the last half of the experiment (Table 9, "Overall-2nd"). It is not clear why anxious participants did so. Although FMT power was correlated across subjects with the effort bias (see below) similarly to correlation between anxiety scores and effort bias (i.e., increased FMT was associated with increased effort bias, whereas increased anxiety scores were associated with reduced effort bias), anxiety scores were not related to FMT. One possibility is that, as their muscles fatigued with time on task, concern about whether the effortful choice would be successful led anxious participants to avoid selecting those choices.

The effort production task elicited a standard RewP, albeit one that was somewhat smaller than observed in other commonly used RewP tasks (e.g., -3.9 µV here vs. -7.6 µV in Experiment 2). I expected to find a larger RewP following effortful behaviors, when ACC should be most strongly engaged. Partly supporting this prediction, only the high-effort choices but not the low-effort choices elicited a RewP with the characteristic frontal-central scalp distribution. However, RewP amplitude following the easy and the hard choices was not significantly different from each other, perhaps because the task produced smaller RewPs than what is commonly observed to begin with (see Experiment 2). Moreover, the task required participants to freely select between the two effort choices, and there were too few trials to create ERP averages to some choice conditions for some of the participants. Hence statistical power may have been weaker in the between-choice comparison. However, note that the non-frontal-central scalp distribution may indicate that the ACC was less engaged during low-effort choices than during high-effort choices, yet, I cannot exclude the possibility that it was due to the smaller potential rewards in the former than in the latter choices. As expected, participants high in depression scores produced smaller overall RewPs, which was particularly true for feedback following hard choices as compared to easy choices. Taken in the context of their choice behavior, these results indicate that participants high in depression scores were less likely to choose to expend effort, but when they did so, the neural response to rewards was relatively weak. Further, as discussed above, they were especially unlikely to select the effort choice on trials when the rewards were most probable. These observations suggest that individuals high in depression scores are not motivated to engage in effortful behavior because they derive less reward value from doing so, and are therefore discouraged from seeking rewards.

By contrast, the participants who scored high in anxiety produced larger RewPs. Anxiety-related personality traits generally do not affect RewP amplitude, and this result further supports the current literature that blunted RewP is associated with depression which is not influenced by the presence of co-morbid anxiety symptoms (Proudfit, 2015; Weinberg et al., 2012); rather, anxiety has been more consistently associated with a different ERP component that is produced at the time of error (the “error-related negativity”; Moser, Moran, Schroder, Donnellan, & Yeung, 2013). Participants high in persistence also produced larger RewPs, indicating their reward sensitivity particularly during effortful behavior. More difficult to explain is that apathetic participants also produced a larger RewP. Follow-up analyses indicated that the effect of persistence and apathy on RewP amplitude emerged only if these traits were entered into the regression model together. Therefore, this result should be interpreted with caution until more investigations are conducted.

Although FMT power and task performance are not always correlated (e.g., Experiment 2), in the present study, increased FMT power during the choice period was positively correlated with a larger effort bias in the last half of the experiment, consistent with the proposal that heightened FMT power reflects enhanced deployment of cognitive control (e.g., Cavanagh & Shackman, 2015). The FMT ratio (which compares FMT power on easy choice vs. hard choice trials) also corresponded positively to the effort bias. It may be that FMT is more strongly engaged in tasks that demand physical effort as opposed to cognitive effort. It is worth emphasizing that FMT power was assessed during the choice period rather than during the execution period, so the correlation of FMT power with effort bias suggests that a fixed level of cognitive control may be needed to *select* effort actions independent of their execution. Unlike Experiment 2, however, individual personality questionnaires did not predict FMT. A limitation of this study is that the participants were generally more likely to choose the high-effort choice than the low-effort choice (as evident in the 50% reward probability condition), which may have limited the range of individual differences in behavior. Also, differences in the potential reward size were not taken into account in the analyses, which could reveal interesting relationships between task performance and individual differences in personality. These limitations should be considered in future investigations.

Experiment 4

The HRL-ACC theory holds that ACC motivates task selection and maintenance of extended behavior based on learned task values (Holroyd & McClure, 2015; Holroyd & Yeung, 2012). So far in this thesis I have examined the role of ACC as regards to the latter process: maintaining extended behavior. But the theory also posits that ACC is involved in motivating task selection, which is conducted in a hierarchical manner by different subdivisions within the ACC (Holroyd & McClure, 2015). My discussion thus far has been specific to a dorsal and caudal subdivision of ACC (i.e., dACC), which is hypothesized to learn option-specific values and to motivate task selection according to those values: for example, should I analyze my data more or write a thesis chapter? On this view, the dACC applies control signals that sustain task performance, ensuring that other brain areas (such as DLPFC and basal ganglia) execute option-specific primitive actions (like entering numbers into MATLAB for analyses). Problematically, however, the application of control can make task switching harder; as will be explained below, SCs are believed to arise from control over task execution (see Monsell, 2003). A computational model based on the HRL-ACC theory posits that SCs impose a penalty that make it more difficult for dACC to switch between tasks, even if a potential task has a higher reward value than the current task under execution (Holroyd & McClure, 2015). Meanwhile, on this view the rostral subdivision of ACC (i.e., rACC) is hypothesized to learn the value of a higher-level task goal (or “meta-option”) (e.g., Is it worth working tonight?) by averaging rewards received across options, which are utilized to regulate control over dACC. According to this view rACC ramps up and down control levels according to the average reward value of the meta-option, increasing control when the received rewards are less than the average reward value (e.g., following errors) and decreasing control otherwise (e.g., when performance is good). Further, rACC’s control signal over dACC is said to attenuate SCs, thereby facilitating task switches within the domain of the meta-option (e.g., entering data, creating graphs, writing the results section, etc). Previous findings are consistent with this hypothesis, showing efficient task switching ability with increased rACC activity but perseveration when rACC is impaired

(Gläscher, et al., 2012; Holroyd & McClure, 2015; Wager et al., 2005; see also Pollmann et al., 2000).

These considerations suggest that task switching performance should be associated with personality traits related to ACC function such as persistence (Blanchard et al., 2015; Gusnard et al., 2003; Kurniawan et al., 2010; Parvisi et al., 2013) and reward sensitivity (Bress & Hajcak, 2013; Keedwell et al., 2005; Liu et al., 2014; Pizzagalli, 2011). Moreover, rumination – a repetitive, maladaptive thinking style about oneself – is closely related to depression (Nolen-Hoeksema, 1991), and has been associated with perseveration and impaired task switching ability (Altamirano, Miyake, & Whitmer, 2010; Davis & Nolen-Hoeksema, 2000; Whitmer & Banich, 2007). Therefore, in the current study I utilized a task switching paradigm to investigate how these personality traits were associated with task selection as predicted by the HRL-ACC theory.

The task switching paradigm typically requires participants to switch back and forth between two simple tasks. Among a variety of task switching designs, a common approach depends on cues that inform participants what task to perform on a given trial (Meiran, 1996; Monsell, 2003). Despite differences in the methodologies, the standard finding is that when participants switch tasks, RTs are slower and errors are more likely as compared to when they repeat the same task, a phenomenon known as the SC (Allport, Styles, & Hsieh, 1994; Jersild, 1927; Meiran, 1996; Rogers & Monsell, 1995; Spector & Bierderman, 1976). Although the underlying mechanisms of SCs are still highly debated, a commonly accepted theory relates the phenomenon to the concept of "task-sets", which have been defined as "a configuration of cognitive processes that is actively maintained for subsequent task performance" (Sakai, 2008). It has been proposed that SCs occur because of the need to re-configure task-sets when tasks switch between consecutive trials, which is not the case when the same task is repeated (Monsell, 2003). More interestingly, yet seemingly paradoxically, numerous studies have reported larger SCs when participants switched to easier, more automatic tasks (e.g., the word reading task in the Stroop task) compared to when they switched to harder, more effortful tasks (e.g., the color naming task in the Stroop task). It has been proposed that this "paradoxical" asymmetrical SC results from the need to release a residual control bias toward the harder task when switching to the easier task, while no such release of control is necessary when switching from the un-controlled easier task to the harder controlled task (Gillbert & Shallice, 2002; Monsell, 2003; Yeung & Monsell, 2003; but see also Kiesel et al., 2010).

The link between cognitive control and HRL suggests that task selection and the degree of top-down control applied over task performance would be influenced by motivation. Consistent with this supposition, my previous work (Umemoto & Holroyd, 2014) reported a motivational effect of reward on dynamic shifts in control over task execution, which importantly, did not result from strengthening of stimulus-response mappings but rather to enhanced representations of the rewarded task-set itself. Likewise, a number of studies have reported that the impact of motivation on cognitive control varies according to individual differences in motivation (Westbrook et al., 2013) and reward sensitivity (e.g., Braem et al., 2012; Engelmann et al., 2009; Locke & Braver, 2008), highlighting the effects of reward on enhancing task performance. Here I investigated the proposal that particular personality traits should relate to ACC function by utilizing a voluntary task switching paradigm, with a specific interest in the differential role of rACC and dACC in task selection and the degree of control applied over task execution (Holroyd & Yeung, 2012; Holroyd & McClure, 2015). The voluntary task switching paradigm allows participants to freely choose which of two tasks to perform on each trial, under the constraints that both tasks should be performed about equally often and that the tasks should be selected at random as though flipping a coin on each trial (Arrington & Logan, 2004, 2005; Yeung, 2010). Importantly, this paradigm provides a further indication of the impact of paradoxical asymmetrical SCs on behavior: The cost of switching to the easier task is so strong that participants actually choose to perform the harder tasks more often than they choose to perform the easier tasks (Yeung, 2010; Millington, Poljac, & Yeung, 2013; see also Arrington & Logan, 2004). I favored this paradigm over the more common task switching paradigm that utilizes external cues that specify which task to perform because ACC is more strongly involved in voluntary task selection (e.g., Deiber, Honda, Ibañez, Sadato, & Hallett, 1999; Forstmann, Brass, Koch, & Von Cramon, 2006; Vassena, Krebs, Silvetti, Fias, & Verguts, 2014).

Based on the previous literature that rumination is mediated by rACC (see Pizzagalli, 2011), and is associated with perseveration (Altamirano, Miyake, & Whitmer, 2010; Davis & Nolen-Hoeksema, 2000; Whitmer & Banich, 2007), I reasoned that individual differences in rumination should be associated with impaired rACC activity as it would be evident in a task switching paradigm. In line with the theory of Holroyd & McClure (2015), I hypothesized that if rACC activation reduces SCs by applying control over task selection by dACC, then individuals high in rumination would exhibit larger SCs, particularly for the easier task associated with stronger SCs (i.e., larger "paradoxical" asymmetrical SCs), and this would cause high ruminators to more likely stay on the harder task to avoid the high cost of switching to the easier task. I also predicted that motivational traits (i.e., persistence and apathy) and reward sensitivity (i.e., anhedonia) would be associated with increased (persistence) and decreased (apathy and anhedonia) application of top-down control over task performance as revealed by the pattern of SCs. As it has been suggested that SCs arise due to the exertion of control over task execution, individuals high in motivation (i.e., persistence) may produce larger SCs, while those low in motivation (i.e., apathy and anhedonia) may exhibit reduced SCs as little control over tasks is generated (but at the cost of increased errors). Further, note that I did not examine depression symptoms directly in this study; rather, rumination was examined as a symptom of depression (see Nolen-Hoeksema, 1991) because I predicted that this particular symptom of depression should be closely related to rACC activity, as discussed above.

I also utilized the Big 5 personality inventory to examine how the ACC-related traits above aligned with more commonly studied personality traits related to reward and/or affect sensitivity and motivation. For instance, extroversion is characterized by increased positive affect while neuroticism is characterized by increased negative affect (Watson & Clark, 1992). Accordingly, extroversion is associated with enhanced cortical areas associated with reward sensitivity (e.g., OFC) as observed in fMRI (DeYoung, Hirsh, Shane, Papademetris, Rajeevan, & Gray, 2010) and in ERPs (i.e., increased RewP; Cooper, Duke, Pickering, & Smillie, 2014). Extroversion correlates negatively with both depression and anxiety symptoms, while neuroticism correlates positively with these symptoms (Jylhä & Isometsä, 2006) and is believed to reflect a predispositional vulnerability factor for these disorders (e.g., Segerstrom, Tsao, Alden, Craske, 2000; Watson and Clark, 1997). Moreover, conscientiousness is closely related to persistence (Cloninger et al., 1993), and has been associated with increased ACC activity (Gusnard et al., 2003). Therefore, the Big 5 personality traits were expected to complement the relation between the ACC-related traits and task performance.

Materials and methods

Participants

We ran two versions of the task, with the second being a slightly modified version of the first (see below). One hundred and thirty-two undergraduate students participated: 57 of them (15 male) participated in version 1 and 75 (17 male) undergraduate students participated in version 2. Participants were recruited from the University of Victoria Department of Psychology subject pool to fulfill a course requirement. All subjects (32 males, age range=18-33 years, mean age =21 +/- 3 years) had normal or corrected-to-normal vision. All subjects provided informed consent as approved by the local research ethics committee. The experiment was conducted in accordance with the ethical standards prescribed in the 1964 Declaration of Helsinki.

Task Design

Participants performed a voluntary task switching task (Yeung, 2010) in which they freely chose to respond to a given stimulus either based on its location (location task) or on its shape (shape task). On each trial, one of three shapes (a circle, a square, or a triangle) appeared in one of three locations inside a grid composed of three adjacent boxes (5.5 cm by 15 cm) (Figure 20). The stimulus and location were pseudo-randomly selected such that each shape was equally likely to appear in each of the three grids. Half of the participants used their right (left) hand to respond to the shape of the stimulus and their left (right) hand to respond to the location of the stimulus. Participants used the three middle fingers (i.e., the index, middle, and ring fingers) of each hand to respond to the stimulus by pressing either of the “Q”, “W”, and “E” keys with their left hand or the “P”, “[“, and “]” keys with their right hand on a standard keyboard. Stimulus-response mappings were compatible for the location task, such that participants used their leftmost finger for the stimulus appearing in the left box, their middle finger for the stimulus appearing in the middle box, and their rightmost finger for the stimulus appearing in the right box. For the shape task, the leftmost finger was always used for the circle, the middle finger for the square, and the rightmost finger for the triangle. Each block of trials started with presentation of the grid, which remained on the screen throughout the block. Each trial started with the shape stimulus appearing in one of the locations within the grid and remained on the screen until participants made a response. The next trial began 200 ms after participants had responded with a presentation of the next stimulus; stimulus repetitions were possible (i.e., the same stimulus could appear in the same location consecutively across two trials).

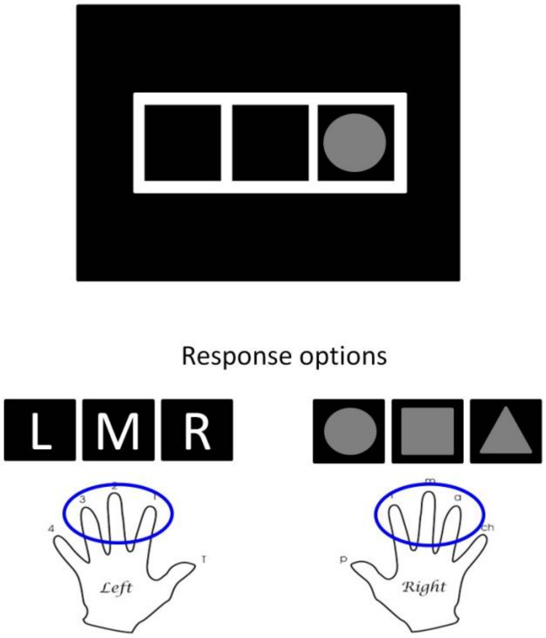


Figure 20. An example trial in Experiment 4. In this example, three middle fingers of the right hand were used to respond to the shape of the stimulus (circle, square, and triangle from the left-most finger to the right-most finger) and three middle fingers of the left hand were used to respond to the location of the stimulus (left, "L", middle, "M", and right, "R", from the left-most finger to the right-most finger). The task-hand mapping was counterbalanced across participants (see text). Here if a participant decides to respond to the shape, the correct response is to use the left-most finger of the right hand (i.e.,

corresponding to the circle). If a participant instead decides to respond to the location of the stimulus, the correct answer is to use the right-most finger of the left hand (i.e., corresponding to the right location).

Procedure

Participants first practiced each task separately (27 trials each). They then practiced switching between the two tasks within the same block of trials (two blocks of 45 trials each) with the following instruction (adapted from Yeung, 2010):

> For the rest of the experiment, you'll be asked to switch back and forth between the Shape and Location tasks. You only need to do one task on each trial—that is, you only need to press one button for each shape you see. In fact, you have to choose which task to perform on each trial. You should perform each task on about half the trials, and you should try to perform the tasks in a random order. For example, imagine you have a coin that said "shape" on one side and "location" on the other. Try to perform the tasks as if flipping the coin decided which task to perform. So sometimes you will be repeating tasks, and sometimes you will be switching tasks. We don't want you to count the number of times you've done each task or alternate strictly between tasks to be sure you do each one half the time. Just try to do them randomly.

After each block of practice trials participants received feedback regarding their average RT and accuracy. When switching between tasks during the practice blocks, they were further informed about the proportion of trials that they chose the shape and the location tasks, as well as how often they switched between tasks. They were also reminded to perform the task quickly and accurately, and that the two tasks should be performed about equally often by switching back and forth between them. The feedback on RT and accuracy were provided in order to ensure that the participants remained engaged in the task while adhering to the task instructions described above. For instance, switching tasks half-way through the experiment would result in performing the two tasks equally often but would defeat the point of the study, which is about task-switching. A strategy of systematically alternating between the two tasks would also fail to comply with the instructions because in that case the subjects would not be choosing the tasks at random. Therefore, participants were discouraged from using these strategies. The experiment proper, which was comprised of 8 blocks of 90 trials each, began following the practice period. Two groups of participants performed slightly different versions of the task. Fifty-seven participants performed the task in a single room in our laboratory (version 1) and 75 participants performed the experiment in groups of up to 10 participants in a computer laboratory at the University of Victoria (Version 2). For both groups performance feedback was provided after each block of trials as in the practice block, except the group performing version 2 did not receive feedback on the proportion of trials selected for each task. Finally, participants in both versions performed a random number generation task following the completion of the task switching experiment, but these results were not analyzed for the current study.

Questionnaires

Following task completion participants answered five personality questionnaires administered via LimeSurvey on the same computer where the task was performed. These questionnaires included the 20-item Persistence Scale (Cloninger et al., 1993), the 22-item Ruminative Responses Scale (Nolen-Hoeksema et al., 1994), the 14-item Apathy Scale (Starkstein et al., 1992), the 14-item Snaith-Hamilton Pleasure Scale (SHAPS, Snaith et al., 1995), which assesses the level of anhedonia, and the 44-item Big 5 Personality Inventory, which assesses 5 core personality factors (openness, conscientiousness, extroversion, agreeableness, and neuroticism) (John, 1990). Each questionnaire was answered on a Likert-scale ranging: from 1 (definitely false) to 5 (definitely true) for the Persistence Scale, from 1 (almost never) to 4 (almost always) for the RRS, from 1 (strongly/definitely agree) to 4 (strongly disagree) for the SHAPS, from 1 (not at all) to 4 (a lot) for the Apathy Scale, and from 1 (disagree strongly) to 5 (agree strongly) for the Big 5 Personality Inventory. Higher scores indicated higher levels on these traits (i.e., high in persistence, rumination, anhedonia, apathy, and the 5 personality factors in Big 5).

Statistical Analyses

The first trial of each block, error trials, trials following errors (for the RT analyses only), and trials with response repetitions were excluded from statistical analysis. Response repetitions have been commonly excluded from statistical analyses in task switching studies (e.g., Bryck & Mayer, 2008; Yeung, 2010; Yeung & Monsell, 2003) because they can differentially affect switch and repeat trials (i.e., on the SCs), particularly when using two tasks that differ in task difficulty. Trials with RT +/- 2 standard deviations (SD) of the RTs for each subject were also eliminated from analysis to eliminate the effect of outliers on average RTs. SCs were calculated for each measure as switch trials minus repeat trials, separately for the two tasks (i.e., *SC-shape*, the location-to-shape switch trials minus the shape-to-shape repeat trials, and *SC-location*, the shape-to-location switch trials minus the location-to-location repeat trials), separately for RTs and error rates. SCs for the two tasks were also averaged together to create *average SCs*, separately for RTs and error rates. Additionally, SCs for the shape task was subtracted from SCs for the location task to generate a difference in SC (i.e., asymmetrical SCs), separately for the RTs and error rates. The task bias was measured as in the previous studies (Arrington & Logan, 2004; Millington, Poljac, Yeung, 2013; Yeung, 2010) by taking the difference between the proportions of trials participants spent on the shape task and on the location task, with larger values indicating that participants chose the harder shape task more often than the easier location task. Data were combined across the two versions of the task to increase the statistical power[5].

I also created a combined measure of RTs and error rates in order to address possible speed-accuracy trade-offs between these measures. First, to generate an *overall performance* measure, the average RTs and error rates across the two tasks for each participant were separately z-scored across participants. Then, the standardized values were added together for each participant, such that higher values indicate worse performance (i.e., longer RTs and increased error rates). Second, to generate an *overall SC*, the average RT-SCs to the shape and to the location task for each participant were pooled into a single distribution across participants. These values were then z-scored across participants, and subsequently sorted back into separate distributions for shape and

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[5] The two versions yielded similar results except that the average RT for the 1st version was statistically significantly slower than the 2nd version by 68 ms (p=.02).

location. This procedure was then repeated on the error rate-SCs to the shape and location task. Finally, the standardized RT-SCs and error rate-SCs were summed together for each participant, separately for the shape and location tasks, thereby generating an *overall SC-shape* and *overall SC-location* measures. Standardization this way ensured that the standard phenomena associated with task switching paradigm (in particular, asymmetrical SCs between tasks with varying difficulty) did not reflect simple speed-accuracy trade-offs. Moreover, the difference in the overall SCs (i.e., asymmetry in the overall SCs) was calculated by subtracting the overall SC-shape from the overall SC-location. Larger values indicate larger asymmetry in SCs between the two tasks (i.e., larger overall SCs-location than the overall SCs-shape).

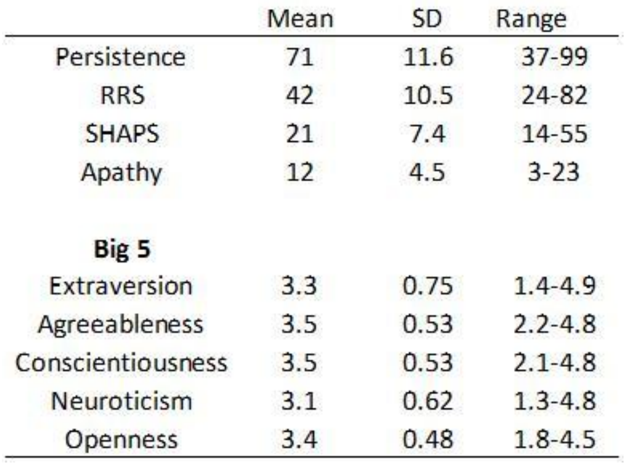
A multiple linear regression analysis was conducted on the overall performance measure and overall SCs (i.e., the standardized performance measures), and on the proportion of switch trials with the personality traits as predictors (including the Persistence Scale, RRS, Apathy Scale, SHAPS, and the 5 factors from the Big 5 personality inventory as indicated above), as well as on the trait persistence using the same method as in Experiments 1-3 (see Experiment 1 for the detail). Outliers were treated as described in the introduction to the thesis.

Results

Participant exclusion criteria included multiple major concussions/acquired brain injury (2 participants), difficulty understanding the task instructions in English (5 participants), and responses that consisted of more than 30% errors (1 participant), leaving the data of 124 participants total for analysis. In addition, for the error analyses only, the data of 10 more participants were excluded due to a technical error, leaving the data of 114 participants total for the error-related analyses (and combined RT-error analyses).

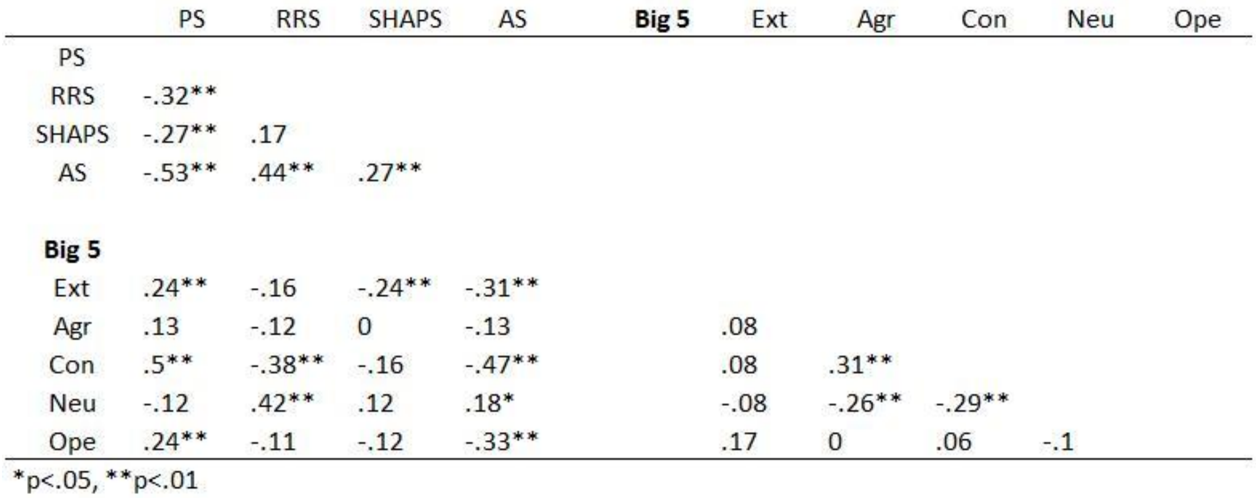
Questionnaires

A summary of the personality questionnaire scores is provided in Table 11, and a summary of zero-order correlations among these questionnaires is provided in Table 12.



	Mean	SD	Range
Persistence	71	11.6	37-99
RRS	42	10.5	24-82
SHAPS	21	7.4	14-55
Apathy	12	4.5	3-23
Big 5			
Extraversion	3.3	0.75	1.4-4.9
Agreeableness	3.5	0.53	2.2-4.8
Conscientiousness	3.5	0.53	2.1-4.8
Neuroticism	3.1	0.62	1.3-4.8
Openness	3.4	0.48	1.8-4.5

Table 11. A summary of participant personality questionnaire scores in Experiment 4. RRS=ruminative responses scale. SHAPS=Snaith-Hamilton pleasure scale.



	PS	RRS	SHAPS	AS	**Big 5**	Ext	Agr	Con	Neu	Ope
PS										
RRS	-.32**									
SHAPS	-.27**	.17								
AS	-.53**	.44**	.27**							
Big 5										
Ext	.24**	-.16	-.24**	-.31**						
Agr	.13	-.12	0	-.13		.08				
Con	.5**	-.38**	-.16	-.47**		.08	.31**			
Neu	-.12	.42**	.12	.18*		-.08	-.26**	-.29**		
Ope	.24**	-.11	-.12	-.33**		.17	0	.06	-.1	

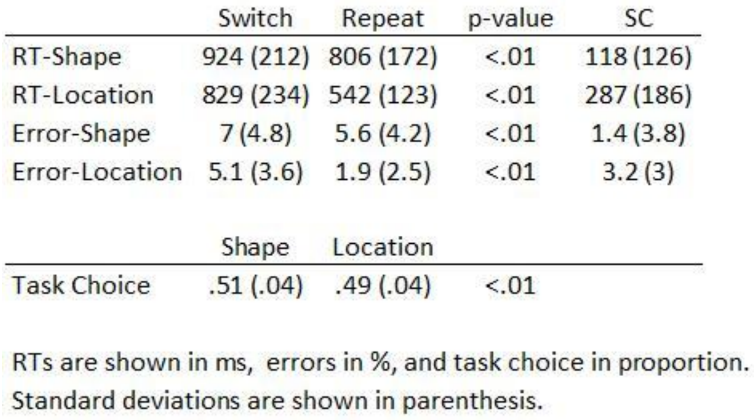
*p<.05, **p<.01

Table 12. A summary of zero-order correlations among the personality questionnaires. PS=persistence scale. RRS=ruminative responses scale. SHAPS=Snaith-Hamilton pleasure scale. AS=apathy scale. From the Big 5 personality inventory: Ext=extroversion. Agr=agreeableness. Con=conscientiousness. Neu=neuroticism. Ope=openness.

Behaviors

Table 13 shows the means and SDs for the shape and the location task. As expected, the location task was performed faster and with fewer errors compared to the shape task (RTs: t(123)=18.9, p<.01, and error rates: t(113)=9.9, p<.01), indicating that the location task was easier than the shape task (Figure 21a & b). I replicated significant

SCs for RT (Figure 21a) such that switch trials were slower than the repeat trials for both the shape task, t(123)=-10.4, p<.01, and the location task, t(123)=-17.1, p<.01. Likewise, SCs for the error rates were significant (Figure 21b), such that switch trials produced more errors than the repeat trials for both the shape task, t(113)=-4, p<.01, and the location task, t(113)=-11.1, p<.01. As expected, SCs were asymmetrical between the two tasks so that the SCs to the location task were larger than the SCs to the shape task for both RTs, t(123)=-11.9, p<.01, and error rates, t(113)=-4.2, p<.01 (Figure 21c & 21d). Consistent with these observations, the overall SCs-location (combined across the RT and error rates data), t(113)=5.7, p<.01, and overall SC-shape (combined across the RT and error rates data), t(113)=-5.8, p<.01, were significant, indicating that the findings do not result from a speed-accuracy trade-off (Figure 21e). Furthermore, the overall SCs-location was significantly larger than the overall SCs-shape, t(113)=-9.2, p<.01, confirming that the asymmetry in SCs was not due to a speed-accuracy trade off. Finally, I also replicated a small but significant task selection bias, indicating that participants chose the shape task more often than the location task (Table 13), t(123)=3.5, p<.01. Thus, consistent with previous studies (Yeung 2010; Millington et al., 2013), I replicated the finding that participants voluntarily selected the harder (shape) task more often than the easier (location) task.



	Switch	Repeat	p-value	SC
RT-Shape	924 (212)	806 (172)	<.01	118 (126)
RT-Location	829 (234)	542 (123)	<.01	287 (186)
Error-Shape	7 (4.8)	5.6 (4.2)	<.01	1.4 (3.8)
Error-Location	5.1 (3.6)	1.9 (2.5)	<.01	3.2 (3)

	Shape	Location	
Task Choice	.51 (.04)	.49 (.04)	<.01

RTs are shown in ms, errors in %, and task choice in proportion.
Standard deviations are shown in parenthesis.

Table 13. A summary of the means and standard deviations for each condition for the two tasks. Task choice represents the proportion of trials each task was performed.

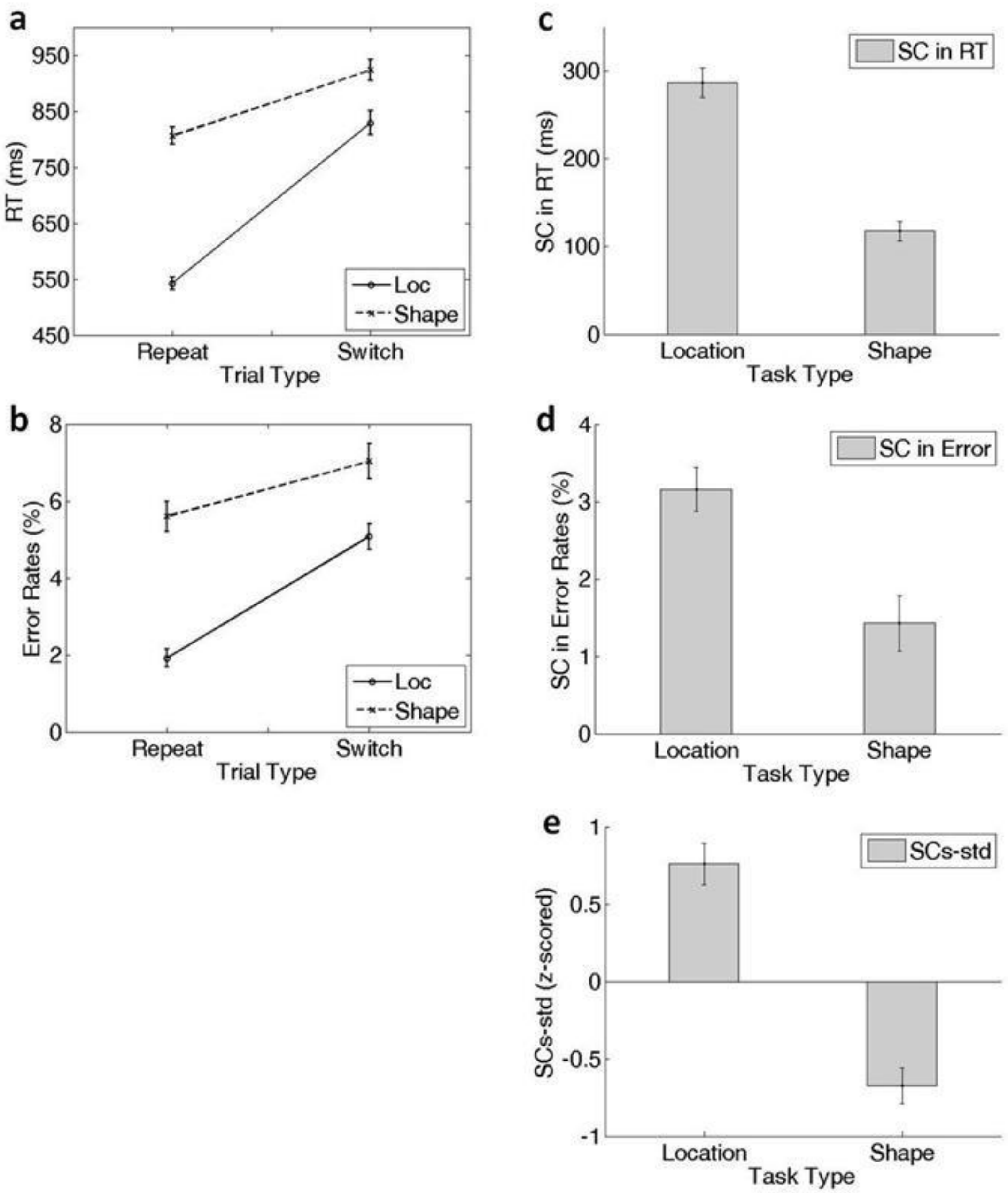


Figure 21. The results of task performance. (a) Reaction times (RTs) in milliseconds (ms) for the repeat and switch trials (x-axis) for the location (Loc) and the shape task. (b) Error rates (%) for the repeat and switch trials (x-axis) for the location (Loc) and the shape task. (c) Switch costs (SCs) in RT to the location (left) and the shape (right) task. (d) Switch costs (SCs) in error rates to the location (left) and the shape (right) task. (e) The standardized SCs (SCs-std), combined across the RT and error rates data, for the location (left) and the shape (right) task. Error bars indicate within-subject standard errors of the mean.

Relations between behaviors and questionnaire scores

Table 14 provides a summary of multiple regression results on the overall performance measure and the overall SCs, which incorporated both RTs and errors, thereby accounting for speed-accuracy trade-offs. A multiple regression analysis on the overall performance measure indicated that participants high in extroversion, neuroticism, and persistence performed the task worse, F(3,107)=4.3, p=.01, accounting for 11% of the variance. Comparable analyses indicated that overall SCs were larger for participants high in extroversion and agreeableness, F(2,111)=9.4, p<.01, explaining 15% of the variance, and larger asymmetrical SCs for participants high in extroversion and neuroticism and low in persistence, F(3,108)=3.8, p=.01, explaining 10% of the variance. To examine whether participants differed on the likelihood for switching between tasks, a multiple regression analysis was conducted on the proportion of trials participants switched between tasks, which revealed that participants high in extroversion and anhedonia were significantly less likely to switch tasks compared to their counterparts, F(2,118)=7.4, p<.01, explaining 11% of the variance (Table 14). No personality traits predicted the proportion of trials one task was chosen over another task (i.e., the task bias). However, as an exploratory analysis, a multiple regression analysis was conducted on the trait persistence scores with the remaining personality trait scores, the difference in the overall SCs (i.e., the asymmetry in the overall SCs between tasks), and the task bias as predictors indicated that participants high in conscientiousness and low in anhedonia, apathy, the overall difference in SCs, and the task bias showed increased persistence, F(5,108)=15, p<.01, explaining 41% of the variance (Figure 22).

Multiple linear regression on task performance

	Predictors	Beta	t	p-value	Final model	R²
Overall Performance	Extroversion	0.21	2.3	0.03	F(3,107)=4.3, p=.01	0.11
	Neuroticsm	0.17	1.9	0.06		
	Persistence	0.17	1.8	0.08		
Overall SCs	Extroversion	0.21	2.4	0.02	F(2,111)=9.4, p<.01	0.15
	Agreeableness	0.3	3.4	<.01		
Overall diff-SCs	Extroversion	0.17	1.8	0.07	F(3,108)=3.8, p=.01	0.1
	Neuroticsm	0.2	2.2	0.03		
	Persistence	-0.18	-2	0.05		
Proportion Switch	Extroversion	-0.33	-3.7	<.01	F(2,118)=7.4, p<.01	0.11
	Anhedonia	-0.19	-2.1	0.04		
Persistence	Conscientiousness	0.35	4.2	<.01	F(5,108)=15, p<.01	0.41
	Anhedonia	-0.14	-1.8	0.07		
	Apathy	-0.32	-3.7	<.01		
	Overall diff-SCs	-0.13	-1.7	0.09		
	Task Bias	-0.14	-1.9	0.07		

Table 14. A summary of multiple regression analyses on the overall performance measure, overall SCs, overall difference in SCs (Overall diff-SCs) (i.e., asymmetrical SCs), proportion of trials participants switched tasks (Proportion Switch), and trait persistence. Note that the overall performance measure and overall SCs incorporated both RTs and error rates (see Statistical Analyses).

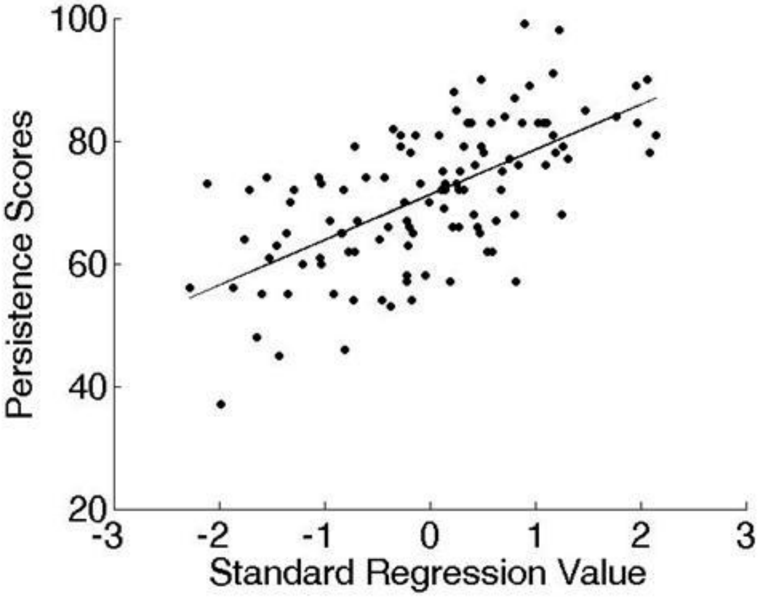


Figure 22. The result of a multiple linear regression analysis on the trait persistence (y-axis) with conscientiousness, anhedonia, apathy, the overall difference in SCs (i.e., asymmetrical SCs), and the task bias, together (i.e., the standard regression value on the x-axis) explaining 41% of the variance.

Discussion

The HRL-ACC theory holds that tasks are selected according to a hierarchical mechanism organized across two subdivisions of ACC (Holroyd & McClure, 2015; Holroyd & Yeung, 2012). First, the dACC is said to apply control signals that sustain task performance; as a consequence, control over task execution prevents against dynamic shifts between different tasks (such as switching between the shape and location task in the present study) that belong to the domain of a given meta-option (such as participating in a psychology experiment). This proposal is consistent with the SC phenomenon observed in task switching paradigms, about which it has been posited that the application of cognitive control can impair performance when participants switch between tasks as compared to when they repeat the same task (Monsell, 2003). Moreover, it has been suggested that greater application of top-down control leads to larger SCs, as indicated by the so-called paradoxical asymmetrical SCs in which switching to an easier task induces larger SCs than when switching to a harder task—which is evidently due to the need to disengage residual control over the harder task. A computational model based on the HRL-ACC theory incorporates these observations by imposing a penalty that impedes dACC from switching between tasks, even when an alternative task is associated with a higher reward value than the current task under execution (Holroyd & McClure, 2015). Second, the rACC is said to implement the higher-level meta-option (e.g., complete the experiment successfully) by applying control signals over dACC that attenuate the SCs (Holroyd & McClure, 2015; see also Gläscher, et al., 2012; Wager et al., 2005), thereby facilitating switches by dACC from one task to another. These considerations suggest that task switching performance should relate to particular personality traits associated with ACC function, such as persistence, apathy, reward sensitivity, and rumination. I therefore investigated this question in a voluntary task switching paradigm, which allowed for analyses of task selection and cognitive control as revealed by the pattern of SCs.

I successfully replicated the standard task switching paradigm phenomena: 1) the location task was performed faster and with fewer errors as compared to the shape task, indicating that the former task was easier than the latter task, 2) the switch trials were slower and more error-prone compared to the repeat trials (i.e., SCs), 3) the SCs to the easier location were larger than the SCs to the harder shape task (i.e., paradoxical asymmetrical SCs), and 4) participants were significantly more likely to choose the harder shape task than the easier shape task (i.e., task bias). In order to address possible speed-accuracy trade-offs, the RT and error rate data were also combined into standardized measures (see “Statistical Analyses”) that replicated the above findings, confirming that the standardized approach did not change the overall pattern of result. I therefore used the standardized measures to examine the relation between task performance and personality traits unconfounded by speed-accuracy trade-offs. The Big 5 personality inventory was included in this analysis to compare a profile of commonly studied personality traits with the ACC-related traits examined here.

Although there was no effect of rumination on task performance as I had predicted, a few personality traits emerged as relating to task performance. Persistence was associated with worse overall performance (i.e., increased RTs and error rates) and smaller differences in the overall SCs (i.e., reduced asymmetry in the overall SCs). At first glance these results may appear at odds with the prediction that individuals high in persistence should exert control over task execution, thereby performing the task well, resulting in increased overall SCs, especially when switching to the easier, location task (as it is expected that the harder task requires most top-down control, which has to be overcome when switching to the easier task). The results did not accord with my prediction, however, a possible explanation is as follows. In addition to their instructions toward being fast and accurate, the participants were also told to switch between the tasks about equally often. Formally, this instruction emphasizes the activation of the meta-option (by rACC) that attenuates SCs, which would serve to facilitate shifts from one task to the other (Holroyd & McClure, 2015). Thus, to the extent that these participants complied to the instruction to switch between the tasks about equally, the worse overall performance does not necessarily indicate that they did not do well in the task. Supporting this, the regression analysis on persistence revealed that reduced task bias predicted persistence, indicating that the more persistent participants selected both tasks more equally compared to the other participants. This observation is consistent with a previous fMRI study where increased rACC activation was associated with higher trait persistence (Gusnard et al., 2003), and this would predict greater shifting between tasks for more persistent individuals (Holroyd & McClure, 2015). To be clear, my replication of the standard paradoxical asymmetrical SCs and the task bias indicates that most participants tended to stick with the harder shape task rather than switch to the easier location task, evidently because of the increased SCs to the easier task. By contrast, the opposite was true in participants who self-reported as persistent: for these individuals both the paradoxical asymmetrical SCs and the task bias were reduced. Taken together, these results may indicate that individual differences in persistence are associated with enhanced motivational control. Although the smaller paradoxical asymmetrical SCs may indicate that more persistent participants applied top-down control over not only the harder shape task but also the easier location task, leading to increased SCs to the harder shape task; however, increased top-down control over both tasks would be expected to enhance task performance overall. It may be that worse performance overall is an inevitable consequence in order to shift between tasks in a manner that complies with the instruction to perform both tasks about equally and randomly.

However, an alternative explanation should be noted. It may be that the more persistent participants simply performed the tasks poorly, especially for the harder shape task, due to decreased dACC activation. This would lead to poor task performance overall and reduced SCs (which would result in reduced paradoxical asymmetrical SCs), leading to increased probability switching between tasks (which would result in reduced task bias). However, whether the trait persistence was associated with increased rACC or decreased dACC cannot be differentiated by a behavioral study alone, and a future fMRI experiment to distinguish these possibilities would provide more insight into this relation.

Nevertheless, given that persistence scores were also predicted by high conscientiousness and low anhedonia and apathy, and that the effect of persistence on behavior and electrophysiology in my other dissertation work revealed enhanced reward learning (Experiment 1), increased self-reported task engagement (Experiment 2) and physical effort expenditure (Experiment 3), these observations together support the interpretation that the persistence is associated with enhanced motivational control over task performance. Future experiments utilizing non-behavioral measures would be helpful to further understand the involvement of persistence in task selection and maintenance of "meta-option" during voluntary task switching, as this would particularly predict increased rACC activation (rather than decreased dACC activation) in more persistent individuals. Nevertheless, as this is a post-hoc interpretation, further verification of the study will be necessary.

The emergence of the two personality traits from the Big 5 personality inventory - extroversion and neuroticism – is also interesting as both traits have been associated with ACC function in the previous literature (e.g., Eisenberger et al., 2005; DeYoung et al., 2010; Gray & Braver, 2002). Extroversion was associated with traits scores associated with high motivation (i.e., high persistence and low apathy scores) and high reward sensitivity (i.e., reduced anhedonia scores). This association may suggest that in extroverted participants, dACC would apply relatively more top-down control over task performance, which may account for the observed increases in overall SCs and larger paradoxical asymmetrical SCs in these individuals (because the higher application of top-down control over the harder shape task would make it more difficult to switch to the easier location task). However, high extroversion was also associated with worse overall performance, but unlike persistence, was not associated with any difference in task bias. Interestingly, extroversion was significantly correlated with reduced likelihood of task switching irrespective of which task was being performed. This may imply that the SCs were so large for the extroverted participants that they were unable to switch between the tasks, indicative of reduced rACC activity; alternatively, it could indicate hyperactive dACC in these participants, which would impede task switches (Holroyd & McClure, 2015). As is the case with the persistence results, a future functional neuroimaging experiment could resolve this question.

Although there was no effect of rumination on task performance, rumination was significantly positively correlated with neuroticism, which was associated with impaired task performance as indicated by the overall performance measure and the increased paradoxical asymmetrical SCs. This may indicate that the effect of neuroticism on task performance partly reflects impaired rACC function. In fact, neuroticism was negatively correlated with rACC and positively correlated with dACC in an affect-neutral paradigm (i.e., oddball task) in an fMRI study (Eisenberger et al., 2005; see also DeYoung et al., 2010, and Gray & Braver, 2002). This observation is in line with the idea that task switches to the easier location task, which normally impose a larger SC penalty for most participants, may have been particularly hard for participants high in neuroticism due to decreased rACC activation. Relatedly, it may be the case that rumination scores did not correlate with any of the task performance measures because rumination commonly occurs in a depressive state (Nolen-Hoeksema, 1991). A future study could investigate whether rumination may affect task switching ability if participants are already in such state, or by experimentally inducing a negative mood.

These results point to the need for further research on the issue. Although ACC has been implicated in these personality traits, the activation patterns associated with extroversion and neuroticism within the different subdivisions of the ACC are not always consistent. This inconsistency may reflect differences in task design, as affective or emotional states are known to modulate extroversion and neuroticism (e.g., Gray & Braver, 2002), but the present study did not include an affective component. Further, both traits appear to reflect multiple constructs. For instance, recent evidence suggests that agentic extroversion is related to motivation and reward-seeking behavior mediated by the DA system, while affiliative extroversion is related to pleasant feelings and to enjoyment of social closeness (Smillie, 2013 for review). Likewise, neuroticism is strongly correlated with anxiety and depression symptoms, but these two disorders are also functionally dissociable, as I observed in Experiment 3 (see also, Proudfit, 2015; Weinberg et al., 2012). Therefore, future research should examine which aspects of these traits may be related to task selection and to the application of cognitive control as proposed by the HRL-ACC theory. Experimental manipulation of affective states may also be useful for understanding individual differences in task selection and motivation, as some of the traits included in this study are affect-sensitive. This, as noted above, may partly explain why I failed to observe any effects of rumination on task performance. Finally, it is not clear why overall SCs were higher for participants high in agreeableness.

Likewise, the decreased task switching for participants high in anhedonia and extroversion also require a follow-up fMRI experiment, particularly because this was the results of exploratory analyses. Nevertheless, this study provides a degree of insight into the role of trait persistence in high-level task performance; further examinations of persistence and its involvement in the proposed rACC-dACC functional divisions would be a fascinating next step.

General Discussion

We humans depend heavily on our cognitive control to make decision and execute goal-directed behaviors, without which our behavior would be overpowered by automatic, stimulus-driven responses. In my dissertation, I focused on a brain region most implicated in this crucial process: the ACC. The importance of this region is highlighted by lesion studies demonstrating diminished self-initiated behavior following ACC damage, the most severe form of which results in the near complete absence of speech production and willed actions in the presence of intact motor ability (Damasio & Van Hoesen, 1983; Devinsky, et al., 1995; Nemeth et al., 1988). Decades of research on ACC has narrowly focused on specific aspects of cognitive control to understand the precise function (Botvinick et al., 2001; Holroyd & Coles; see Holroyd & Yeung, 2011 for review), yet none of the existing theories have been able to explain relatively global impairments in behavior following ACC damage. This discrepancy in the literature motivated Holroyd and Yeung (2012) to propose an unified theory of ACC based on recent advancements in RL theory that integrate hierarchically organized, extended behavior (i.e., HRL; Botnivick et al., 2009; Botvinick, 2012). The HRL-ACC theory suggests -- based on a multitude of evidence from animal, lesion, and neuroimaging studies -- that ACC is responsible for learning task values and motivating effortful control over extended, goal-directed behaviors based on those learned task values (Holroyd & Yeung, 2012; Holroyd & McClure, 2015; see also Shenhav et al., 2013). The aim of my dissertation was two-fold: 1) to improve understanding of ACC function from the perspective of HRL-ACC theory, and 2) to elucidate the role of ACC in depression symptoms as investigated by individual differences in personality traits related to motivation and reward sensitivity. This work was motivated by a large number of studies that have indicated that ACC function is abnormal in a number of psychiatric disorders, including depression.

I conducted four experiments in this dissertation. ACC function was examined both behaviorally and electrophysiologically utilizing the EEG technique that allows for temporally precise measurements of continuous changes in neural activity, providing a means to distinguish between distinct psychological events. Several personality traits related to motivation and reward sensitivity were assessed in a population of healthy college students, with a particular focus on depression symptoms. It was hypothesized that these different personality traits express, to greater or lesser degrees across individuals, ACC function, and that their abnormal expression (in particular, atypically low motivation and reward sensitivity) constitute hallmark characteristics of depression. Specifically, the ACC-personality link was examined by investigating distinct aspects of reward processing (Experiment 1), sustained task performance (Experiment 2), decision making on an extended task involving physical effort (Experiment 3), and task selection (Experiment 4).

Experiment 1 revealed that RewP amplitude, a key electrophysiological signature of reward processing by ACC, is sensitive to individual differences in reward valuation, being larger for those high in reward sensitivity and smaller for those high in depression scores, independent of task performance and neural processes related to reward anticipation. Experiment 2 replicated this association between RewP amplitude and personality traits related to reward sensitivity. Although only a statistical trend, the experiment also revealed that depression scores were associated with relative inability to sustain task performance. Depression scores were also predicted by low persistence scores, reduced RewP amplitude and increased FMT power, reflecting a discrepancy between apparent increased levels of fatigue resulting from sustained effortful control and the low reward value associated with task performance, resulting in poor behavioral output. Experiment 3 further replicated the blunted RewP in participants high in depression scores. These individuals also exhibited reduced willingness to expend physical effort, particularly when reward receipt was more likely, a behavior that was stable with time on task. In contrast, individuals characterized by high persistence exhibited increasing effortful behaviors with time on task, particularly for trials in which reward receipt was unlikely. Further, Experiment 4 suggests that participants high in persistence likely adhered to a high-order task instruction about switching between tasks.

The general discussion integrates the rationales and findings of each experiment as they relate to the putative function of ACC and depression symptoms. They will also be discussed in relation to the current literature on the mechanisms of depression. Finally, I will discuss future directions, including a brief note regarding treatments.

Dissecting reward processes

Anhedonia, the cardinal feature of depression, has long been considered to reflect an inability to experience in-the-moment pleasure. However, the evidence now argues against this notion, instead pointing toward a motivational deficit associated with depression. Encouraged by influential research in non-human animals (Berrdge & Robinson, 1998, 2003; Berrdge et al., 2009), many recent studies have compared reward anticipatory process (reward "wanting") with reward consummatory process (reward "liking") associated with depression (Der-Avakian & Markou, 2011; Zhang, Chang, Guo, Zhang, & Wang, 2013), the former of which heavily relies on midbrain DA system (Schultz et al., 1997). Nevertheless, the evidence regarding which aspect of reward processing is abnormal in depression has been inconsistent, which is partly due to current diagnostic approaches that categorize and dichotomize complex mental disorders, to different experimental methodologies and techniques, and to different clinical profiles (e.g., severity, co-morbid disorders) and medication status of participants across studies. One cannot emphasize enough the complexity of mental disorders. In fact, the United States National Institute of Mental Health proposed new ways of studying mental disorders, known as RDoC, so that mental disorders are understood as dimensional traits derived from the operation of basic neurocognitive mechanisms (e.g., brain mechanisms concerned with cognitive control), and dysfunction of these mechanisms give rise to sets of symptoms that cut across multiple disorders (e.g., Insel et al., 2010). Strikingly, ACC is implicated in all five major domains of function currently associated with the RDoC, indicating that precise ACC function is still not fully understood and suggesting that ACC function may mediate a specific construct underlying a range of disorders (Holroyd & Umemoto, 2016).

Based on the recent proposal that ACC learns the values of tasks and motives the execution of those tasks (Holroyd & Yeung, 2012; Holroyd & McClure, 2015), I hypothesized that ACC function should be expressed as individual differences in personality associated with motivation and reward sensitivity, the abnormal expression of which would result in disorders such as depression. Encouraged by the RDoC framework, I investigated individual differences in ACC-related personality traits as they relate to distinct reward processes. A key electrophysiological marker of ACC function, the (feedback-related) RewP, is believed to index the impact of RPE signals carried by midbrain DA neurons on ACC, and RewP amplitude has been considered a potential biomarker for depression (see Proudfit, 2015). Consistent with this proposal, across all three electrophysiological experiments (Experiment 1-3), RewP amplitude was attenuated in individuals with increased depression scores, whereas larger RewPs were produced in individuals high in reward sensitivity (Experiment 1 & 2). What do these observations suggest? The DA RPE signals incorporate hedonic reward values computed by the DA-rich reward-related brain regions, particularly the striatum (including nucleus accumbens) and OFC. As these brain regions critical for reward processing are often hypoactive in depression, reduced (or impaired) reward valuation by these regions would be conveyed as reduced (or abnormal) RPE signals by the DA system, disrupting the saliency of rewards and reward learning. These RPE signals are then carried to ACC, where they elicit a smaller (or abnormal) RewP as seen in individuals with depression or high in depression symptoms. In fact, abnormal RPE signals in depressed individuals have been reported in DA-rich brain regions including ACC (Kumar et al., 2008; see also Gradin et al., 2011). This view – that the DA RPE signals carry information about how much a person *values* given rewards which is computed by such brain regions as above, the impact of which is then conveyed to ACC as indexed by RewP amplitude -- is consistent with the past studies showing that blunted RewPs were normalized by motivationally salient rewards such as the monetary rewards in children with ADHD (Umemoto et al., 2014) and in problem gamblers (Hewig et al., 2010), and drug rewards (i.e., cigarette puffs) in substance dependent individuals (Baker et al., 2015). Furthermore, in my experiments abnormal reward anticipation and poor reward learning did not influence feedback-related RewP, as discussed below, suggesting that RewP reflects individuals' sensitivity to reward, rather than indirectly reflecting other aspects of task performance.

Impaired reward learning was found in individuals high in depression scores in Experiment 1, but only on trials with low reward probability (see also, Pizzagalli et al., 2005, 2008). Because the reward signals were also smaller in these individuals (as indicated by feedback-RewP amplitude), I would expect dACC to have difficulty in integrating these signals to learn the correct response-reward associations, especially for rewards that were only intermittently available (e.g., Kennerley et al., 2006). In contrast, the trait persistence predicted superior reinforcement learning, which is suggestive of good ACC function (see introduction). Further, an extensive body of research indicates that reward anticipation is impaired in depression, but the precise nature of the underlying neural abnormality has yet to be fully understood (Der-Avakian & Markou, 2011; Zhang et al., 2013). The results of Experiment 1 revealed that participants high in depression scores produced increased SPN amplitude overall, indicating a pessimistic view of forthcoming reward delivery, consistent with the traditional view of depression in enhanced attention to negative information (Beck, 1976; De Raedt & Koster, 2010; Matt et al. , 1992). It is worth noting that I observed this pattern of anticipatory processing only during the period when participants awaited reward delivery and not in response to reward predictive cues, the latter of which are often studied as an indicator of reward anticipation in neuroimaging studies (e.g., Knutson et al., 2008; Smoski et al., 2011). The seminal study by Schulz and colleagues (1997) reported that the DA RPE signals at the time of unexpected reward delivery propagate back in time with learning to the earliest indication of rewards. This indicates that if rewards are poorly learned, or RPE signals are small to begin with, it is unlikely that the RPE signals would travel back to reward predictive cues. Examining anticipatory processes in response to different psychological events (i.e., reward predictive stimuli vs. outcome anticipation) may partly explain the inconsistent results regarding reward anticipation in depression. Notably, IU was also associated with abnormal reward anticipation, but the pattern of results differed from those associated with depression symptoms, such that participants high in IU behaved as though they did not care about highly probable, forthcoming negative outcomes, which manifested both in the response to reward predictive cues (by the cue-RewP) and during the delay period prior to reward delivery (by the SPN). Although IU was initially identified in reference to general anxiety disorder, recent thinking suggests that IU can serve as a transdiagnostic construct across anxiety and depression symptoms (Mahoney & McEvoy, 2012; McEvoy & Mahoney, 2012). Despite the positive correlation between IU and depression scores in Experiment 1, these observations indicate distinct contributions of these traits to distinct aspects of reward processing.

ACC's role in effortful control over extended behavior

Despite decades of research into cognitive control processes mediated by ACC, the mechanisms underlying extended behavior have drawn little attention. However, a number of neuroimaging studies have revealed that ACC is activated throughout task performance (Dosenbach et al., 2006. Croxson et al., 2009; see also Holroyd & Yeung, 2012), and that ACC damage results in difficulty in sustaining optimal task performance, reflecting impaired ability to integrate reinforcement episodes across trials in studies involving monkeys (Amiez et al., 2006; Kennerley et al., 2006) and humans (Camille et al., 2011; see also Amiez et al., 2015). Further, it has been suggested that FMT, which originates in ACC, indexes processes related to cognitive control and sustained cognitive effort (for reviews Cavanagh & Frank, 2014; Hsieh & Ranganath, 2014; Mitchell et al., 2008). FMT power also progressively increases with time on task (Barwick et al., 2012; Boksem et al., 2005; Wascher et al., 2014), suggesting that ACC supports sustained, effortful behavior in the face of increasing fatigue or mental challenges. It was hypothesized that this function of ACC should be expressed differently according to individual differences in ACC-related personality traits.

Crucially, these two electrophysiological signatures of ACC function – RewP amplitude and FMT power – were uncorrelated with each other in both the task demanding cognitive effort (Experiment 2) and physical effort (Experiment 3), suggesting that these phenomena index independent aspects of ACC function. As noted above, reward valuation as indicated by feedback-related RewP amplitude was attenuated in individuals high in depression scores across Experiments 1-3. Consistent with a previous suggestion that people high in depression symptoms have difficulty in using reward-related information to motivate behavior (Treadway et al., 2009, 2012), I found these individuals to exhibit relatively poor prolonged task performance in Experiment 2 and a reduced willingness to expend effort to obtain probable rewards in Experiment 3. Fatigue-related decrements in performance on prolonged tasks can normally be restored with sufficiently valuable incentives (Boksem et al., 2006), but this normalization would be unlikely to occur in individuals high in depression symptoms because of their insensitivity to rewards. These observations align with an extensive RL literature suggesting that DA RPE signals are used to translate motivational saliency or reward value into behaviors that maximize the likelihood of future rewards (Holroyd & Coles, 2002; McClure et al., 2003; Montague et al., 2004). More specifically, when reward acquisitions were more likely, or when rewards induced strong desire to obtain them, reward-seeking behavior would naturally increase; however, because of low reward valuation as seen in the smaller RewP, individuals high in depression scores were less likely to choose effortful, yet reward-maximizing behaviors. In contrast, when reward acquisitions were less likely, or when participants were fatigued, reward-seeking behavior would naturally decrease; however, individuals high in reward sensitivity or motivation (i.e., persistence) exhibited increased self-reported task engagement (Experiment 2) and produced more effortful behavior particularly as fatigues increased with time on task (Experiment 3). Interestingly, individuals high in reward sensitivity (i.e., reward responsiveness) who exhibited a large RewP appeared so reward-driven that the receipt of a small reward on about every other trial (i.e., with a 50% reward probability) appeared to be sufficient to sustain a high level of performance on a prolonged task, whereas those characterized by high in-the-moment pleasure (i.e., reward consummation (TEPS-C)) appeared less able to sustain behavior, resulting in progressively increasing FMT power to sustain task performance (Experiment 2).

Although anxiety and depression symptoms often co-occur, the results of Experiment 2 and Experiment 3 (as well as Experiment 1) point to distinct underlying impairments, particularly as revealed by blunted RewP in individuals high in depression scores but not in individuals high in anxiety scores (see also Proudfit, 2015). Previous research has pointed to increased recruitment of cognitive control as seen in FMT in anxious individuals also (Mitchell et al., 2008; Cavanagh & Shackman, 2015); however, this relation exhibited only a statistical trend in an exploratory analysis in Experiment 2. It may be that anxiety scores are more specifically associated with transient modifications of behavior (i.e., trial by trial adjustments in RT or accuracy) in response to uncertain or negative events, which anxious individuals are highly sensitive to (Cavanagh & Shackman, 2015), than with the overall level of effortful control deployed over extended behaviors (Wascher et al., 2014). Although the reason that these individuals selected fewer effortful behaviors with time on task is unclear (Experiment 3), one possibility is that they became increasingly worried about failure as the task progressed, thereby choosing the low-effortful behavior more often to ensure constant reward receipt. In turn, this behavior could have produced a larger RewP in anxious individuals if they thought that they might not have received the rewards if they had chosen the alternative, high-effortful choices. Unexpectedly, however, increased FMT power predicted higher depression scores in Experiment 2, suggesting that participants high in depression scores invested greater effort in carrying out the task, despite relatively worse overall performance, resulting in more fatigue (see also Cléry-Melin et al., 2011). Nevertheless, FMT was not correlated with depression scores or any personality traits in Experiment 3. Thus these observations should be replicated and extended in future experiments.

Task selection mechanisms as an interplay between rACC and dACC

The HRL-ACC theory describes ACC's involvement not only in extended behavior, but also in task selection (Holroyd & McClure, 2015). In particular, distinct, hierarchically-organized functional divisions have been proposed between rACC and dACC. On the one hand dACC facilitates task selection based on learned task values (e.g., by deciding to prepare a salad for dinner), and applies a control signal so that other brain regions such as the basal ganglia carry out each element of the task successfully (e.g., washing lettuce, cutting tomatoes, setting cutlery, and so on). Ironically however, increased recruitment of cognitive control over task execution results in larger SCs, because switching to a different task requires release of control applied to the preceding task (Monsell, 2003). On the other hand, according to the HRL-ACC theory, rACC is responsible for selecting and then applying control over the execution of a superordinate task (such as making a healthy meal at home rather than going out for dinner), across subtasks mediated by dACC (such as deciding to make salad); the rACC control signal facilitates task switching by dACC by attenuating SCs (for example, helping dACC switch from making salad to setting the table). In fact, the evidence suggests efficient task switching with increased rACC activation and perseveration when rACC function is impaired (Gläscher, et al., 2012; Holroyd & McClure, 2015; Wager et al., 2005; see also

Pollmann et al., 2000). Furthermore, when two tasks differ in task difficulty, larger SCs are often observed when participants switch from the more difficult task to the easier task. This so-called paradoxical asymmetrical SC is believed to reflect the disengagement of control applied over the execution of the more difficult task when switching to the easier task (i.e., resulting in larger SCs); as less control is required to execute an easier task, such release of control does not occur when one switches away from the easier task to the more difficult task (i.e., resulting in smaller SCs). This asymmetry in SCs appears to be large enough that, when given a choice, participants actually choose to perform the more difficult task more often than the easier task (i.e., they exhibit a bias in favor of the harder task).

Pizzagalli (2011) proposed that rACC operates as a key hub within the DMN, which is active while individuals are engaged in internally focused, self-referential processing (Broyd et al., 2009; Buckner et al., 2008; Raichle et al., 2001), but is de-activated when they are engaged in goal-oriented behaviors and dACC and DLPFC come online (Corbetta & Shukman, 2002; Sounuga-Barke & Castellanos, 2007). It has been hypothesized that maladaptive rumination in depressed individuals sustain hyperactive affect-related brain regions such as the amygdala, which in turn impedes switches to goal-directed behavior (Pizzagalli, 2011). Based on these proposals, I hypothesized that rACC and dACC function supporting task selection should be associated with individuals differences in personality traits related to motivation and rumination. Particularly, rACC function would be expressed by individual differences in rumination, such that individuals high in rumination would exhibit increased SCs, particularly when they switch to easier tasks (because this is hard to begin with), resulting in increased paradoxical asymmetrical SCs. This would in turn cause high ruminators to be more likely to stay on the harder task to avoid the high cost of switching to the easier task. In contrast, dACC function was predicted to be expressed by individual differences in motivational traits (i.e., high persistence, low apathy and anhedonia) such that individuals high in motivation would exert more control over task execution, resulting in larger overall SCs, whereas their counterparts would exert less control, producing reduced overall SCs at the cost of poor task performance.

The results of Experiment 4 did not support the predictions for rumination. In fact, rumination did not predict any of the task switching performance measures. One possible explanation is that rumination is closely related to depressive states so that its effect may emerge when participants are in a negative mood, or by experimentally inducing such mood. A related possibility is that the task switching paradigm I used was purely cognitive in nature, but the impact of rumination on performance may have been observed if the task required switching between different affective stimuli. By contrast, the result related to persistence was consistent with proposal that persistent individuals would apply increased motivational control over task execution. But, it appeared so specifically at a higher task level formed by a high-order task instruction; all participants were told to perform the task as fast and accurately as possible (a responsibility carried out by low-level motor areas but facilitated by dACC), yet they were also told to randomly select each task, switching equally often between the two (a responsibility carried out by dACC but facilitated by rACC). Persistent participants exhibited smaller paradoxical asymmetrical SCs – the SCs to the harder task and to the easy task were about equally large, possibly indicating that they also applied control over the easier task (but see Discussion in Experiment 4) -- *and* a reduced task bias (i.e., they selected the easier task as often as the harder task). The interpretation that persistent participants likely adhered to the larger task goal (random switching between tasks) is also consistent with the observed positive correlation between persistence and trait conscientiousness (Cloninger et al., 1993). Although the trait persistence is generally associated with dACC function, it may be that rACC activity is higher in persistent individuals for tasks that involve hierarchy as in the voluntary task switching paradigm (i.e., perform tasks fast and accurate < perform both tasks about equally) which is not usually the case as the majority of laboratory-conducted experiments entail simple, single-level performance.

Considerations for multiple statistical tests

Across all experiments a large number of multiple linear regression analyses were conducted, which raises the probability for inflating Type I errors. However, the analyses were separated between hypothesis-driven approach and exploratory analyses, and my main focus was on the former analyses. Across experiments, hypothesis-driven analyses were conducted on measures of overall performance, i.e., measures that were not separated into different conditions. In Experiment 1 these measures consisted of the overall cue-RewP, overall SPN, and overall feedback-RewP. In Experiment 2 these were the average TWS, average RewP, and average FMT. In Experiment 3 these were the overall effort bias, overall RewP, and overall FMT. In Experiment 4, these were the overall assymetrical SCs, overll SCs, and the task bias. Further predictions were based on specific findings from the preivous literature. Because the feedback-related RewP has been associated with increased reward responsivenss and depression scores, analyses on the feedback-related RewP for different conditions (e.g., predicted RewP (Experiment 1) and RewP for the hard choice (Experiment 3) were predicted to be associated with the two traits above. Likewise, a relation between a decreased effort choice bias and increased depression symptoms has been reported previously, particularly when reward probability was high (see Experiment 3), therefore this association was predicted to be replicated in Experiment 3 also. Lastly, because rumination has been associated with impaired rACC function and task switching, I predicted this trait to be associated with increased assymetrical SCs and task bias in Experiment 4. By testing these specific predictions I minimized the probability of committing Type I errors.

In addition, exploratory analyses across all the experiments included analyses on each probability condition in Experiment 1 (e.g., predicted readiness potential) and Experiment 3 (e.g., effort bias for the 20% reward probability condition). In Experiment 2 exploratory analyses included the examination of the effect of combined expression of RewP and FMT on different personality traits (Figure 16), as well as the analysis predicting depression scores. In Experiment 4, an exploratory analysis was conducted on persistence scores. Findings from these exploratory analyses especially warrant replication in future studies.

Finally, note that the approach that I used to treat outliers across all of the experiments (see Introduction) was intended to enhance the statistical stability of my results by minimizing the effect of extreme outliers. By rendering less likely the possibility that any of the results were due to a statistical fluke, this procedure should increase the replicability of my findings.

Future directions

This dissertation emphasizes the importance of understanding the basic function of ACC, which is then used to understand its dysfunction in relation to mental illnesses. Given that mental disorders are extremely heterogeneous and complex, understanding their etiology and the development of novel therapies requires moving beyond black-and-white categorization of individuals into groups. The RDoC research initiative proposes exactly that, the purpose being to “Develop, for research purposes, new ways of classifying mental disorders based on behavioral dimensions and neurobiological measures to bring the power of modern research approaches in genetics, neuroscience, and behavioral science to the problems of mental illness… RDoC research starts with basic mechanisms and studies dysfunctions in these systems as a way to understand homogeneous symptom sets that cut across multiple disorders, rather than starting with clinical symptoms and working backwards” (National Institute of Mental Health). On this view, my work points out that a common currency - ACC function - underlies the symptoms of multiple psychiatric disorders that share dysfunction in reward valuation, utilizing reward value to motivate goal-directed behavior, and sustaining that behavior.

My work corroborates the results of previous studies indicating that individuals with or at risk for depression exhibit blunted neural responses to reward feedback. A series of careful investigations by Hajcak and colleagues demonstrated that a smaller RewP is already evident in children aged 8 and 13, which also predicts the first-onset of depression in adolescent girls over and above the influence of family history, trait neuroticism, and sub-threshold depressive symptoms (Bress et al., 2013). Consistent with this, neuroimaging evidence revealed that the striatum – where reward-related signals are incorporated into RPE signals and carried by DA neurons -- was hypoactive in depressed adolescents, which was accompanied by reduced positive affect (Forbes et al., 2006, 2009). These observations suggest a trait-like characteristic of RewP for depression, and predict that depression may be associated with blunted reward valuation across *any* types of reward. This would distinguish depression from other disorders of reward valuation as RewP amplitude can be normalized by specific, desired rewards such as drug rewards in substance abusers (Baker et al., 2015), and monetary rewards in children with ADHD

(Umemoto et al., 2014) and in problem gamblers (Hewig et al., 2010). However, future studies investigating the specificity of RewP to depression is necessary, as one recent study found a normal RewP among depressed individuals who reported intact mood reactivity to positive events (Foti et al., 2014). This study requires replication, but also raises an important question about how to identify sub-groups of affected individuals who in fact exhibit normal reward sensitivity; particularly, what type of dysfunction underlies their specific form of depression and whether this group of individuals have a better prognosis. Another important question concerns whether RewP amplitude can serve as a stable trait-like marker, or whether it changes according to the course of depression illness. Some evidence suggest that reduced reward responsiveness is not normalized in remitted individuals (Pechtel et al., 2013), and that reward processing remains impaired in these individuals (Ditchter et al., 2012; Santesso et al., 2008). Future studies should examine whether RewP amplitude may indicate the prognosis for depression, being smallest during the depressive episodes, intermediate during remission, and largest in full recovery. It may be that individuals with relatively malleable RewP amplitude are those who have a better prognosis.

A new insight from my dissertation is the observed relation between increased depression scores and increased FMT during prolonged task performance, suggesting that individuals high in depression scores invested greater effort to sustain task performance, as discussed above (Experiment 2). However, the finding was not replicated in Experiment 3, raising an important question for future research regarding what the observed FMT activity indicates and how exactly it relates to depression symptoms. The difference in these results between Experiment 2 and Experiment 3 may be due to the fact that participants high in depression scores could choose not to exert effortful control in Experiment 3, and FMT was associated with greater effort expenditure, whereas they had no choice but to expend effort to complete the task in Experiment 2. Also, FMT power was measured during the 4 second choice period in Experiment 3 rather than across task performance in Experiment 2. It may be that the prolonged maintenance of cognitive effort as indicated by the ongoing FMT power is associated with increased depression scores, but the FMT power needed to *select* an effortful option may tap into different cognitive processes and a specific threshold of FMT power (i.e., baseline activity) across individuals may be necessary to exceed in order to select effortful behavior. Somewhat consistently, a previous study found that a relation between FMT and task performance differed depending on what cognitive processes were involved (e.g., pre-stimulus vs. ongoing FMT) (Wascher et al., 2014). Although this possibility indicates that FMT may underly different constructs, another important consideration is that with practice participants may have already selected which choice to execute long before the choice screen had appeared (e.g., persistent individuals may automatically press the corresponding response key to the hard choice without actively thinking which choice to execute, while individuals high in depression scores may do so for the easy choice), hence reducing a potential association between FMT and personality traits.

Moreover, the increasing FMT with time on task in Experiment 2 may reflect increasing inhibition of mind-wondering with time on task (or self-referential processing) which is commonly associated with rostral ACC activity (Pizzagalli, 2011). And this aspect of FMT may be related to the increased depression scores as maladaptive rumination has been often found in individuals with increased depression symptoms. If this is true, a trial-by-trial analysis on FMT (that quantifies fluctuations in FMT power) and performance (e.g., a large change in response between consecutive trials as an indication of mind-wondering) may yield a stronger association between the FMT-performance relation and depression scores (e.g., Weissman et al., 2006). Similarly, a trial-by-trial analysis on FMT in Experiment 3 may provide a clue as to whether the observed FMT in Experiment 2 and Experiment 3 may actually index the same underlying process; for instance, increased FMT power following the receipt of negative feedback or associated with increased variability in response (reflecting attentional slips) in Experiment 2 and that associated with the selection of effortful behavior in Experiment 3 may reflect a common function of FMT in sustaining effortcul control.

A future study could also examine whether increased FMT in response to a challenging task may predict whether participants choose to expend effortful behavior and how well they could sustain it. One interesting study would be to allow participants to freely decide when to take breaks during the experiment, which may reveal frequent, prolonged self-initiated rests with increased FMT, resulting in difficulty completing a given task. In the domain of depression, one study reported that individuals with depression exhibited difficulty in sustaining positive affect (but not negative affect) as observed in reduced activation of the nucleus accumbens over time (Heller et al., 2009). Closer examination may reveal increased FMT with time on task resulting in reduced capacity to sustain positive affect by ACC. Although extended behavior is rarely studied in relation to depression, I believe that high rates of relapse among the affected individuals may in part be due to poor ability to sustain effortful control over task performance.

A possible link between FMT and depression scores provides insight into another line of research in depression. Numerous studies have reported that increased theta activity in rACC during the resting state predicts positive responses to a variety of treatment options (Pizzagalli, 2011 for review). As rACC at rest is said to play a key role in self-referential processing, a maladaptive form of which is rumination, Pizzagalli suggested that increased resting state theta in rACC may indicate a non-judgemental, adaptive form of thinking about oneself. In view of the results of my dissertation work, I hypothesize that this resting state theta activity may indicate enhanced application of cognitive control by rACC, which is capable of suppressing hyperactive affective regions to which it is directly connected (e.g., the amygdala) and of recruiting dACC and DLPFC for efficient task execution. In the framework of the HRL-ACC theory, this position would predict that increased pre-treatment resting state rACC theta activity would be associated with efficient task switching performance and enhanced task maintenance. As the functional significance of this theta activity has not received much research attention, future studies should focus on this question in order to provide insight into treatment outcomes and their relation to FMT occurring during extended, goal-directed behavior, as in my dissertation work.

Implications for treatment: The first-line option for treating depression has consisted of prescribing pharmacological drugs that target the serotonin system; yet these drugs take time to induce changes in affected individuals, and do not address underlying motivational deficits or impaired reward processing (Nutt et al., 2006; Argyropoulos & Nutt, 2013). More often than not, an effective drug choice depends on extensive trial-and-error process, the results of which do not guarantee satisfactory results. It is unlikely that one single treatment approach can remediate this disorder for all affected individuals, as a multitude of dysfunctional processes – related to emotion, mood, cognitive function, motivation, physiological processes (e.g., hormones and circadian rhythms), stress, psychomotor function, and so on -- underlie depression. My dissertation work, together with the RDoC perspective, points to the importance of examining individual differences in brain mechanisms and their dysfunction. For instance, individuals characterized particularly by blunted reward processing and by reduced evidence of effortful control may benefit more from pharmacological intervention that target the DA system (Argyropoulos & Nutt, 2013). Also, psychotherapy treatment (e.g., cognitive-behavioral therapy) could be tailored to address each individual's specific weakness, such as re-building reward sensitivity or improving maintenance of goal-directed behavior as appropriate. Moreover, meditation has been observed to facilitate self-regulation of emotion and to reduce stress levels, and stronger activity of ACC and other brain regions has been reported in meditators (Hölzel et al., 2007; Lutz, Slagter, Dunne, & Davidson, 2008), possibly via FMT-induced strengthening of connections between ACC and other brain areas (Posner, Tang, & Lynch, 2014). Therefore, meditation practice may be a promising intervention for depression symptoms that regulates maladaptive rumination tendencies and improves focused, sustained behavior.

Concluding remarks

Because ACC activation has been observed across many domains of research, the authors of an article published in the Annals of Improbable Research quipped that "The cingulate cortex does everything" (Gage et al., 2008). The authors applied a mathematical growth function to the increasing number of publications involving the cingulate cortex and predicted that "… between 2050 and 2100, there will be more cingulate publications than there are cells in the cingulate cortex itself… and the cingulate cortex will become self-aware" (pg. 13). My dissertation work does *not* suggest that cingulate cortex does everything; however, the putative function of ACC in high-level cognitive processes – motivating extended, goal-directed behavior based on learned task values -- indicate why ACC lights up in many experimental studies. This theory also explains why many mental disorders are associated with ACC abnormality, ranging from substance abuse, ADHD, schizophrenia, OCD, to depression, which share impairments in various forms in reward valuation, translation of motivational values into goal-directed behaviors, and maintenance of effortful control over those behaviors. In particular, my dissertation work points to blunted reward valuation in individuals high in depression scores, which in turn fail to facilitate extended, goal-directed behavior. It did not appear that these individuals were simply lazy; for instance, they did not report reduced task engagement during the task, and the results instead indicate that they may have found the task especially fatiguing. However, because mental disorders are complex and multiple dysfunctions are likely contributing to them, the apparent abnormality in reward sensitivity and motivational control over behavior should be considered in relation to other dysfunctional processes mentioned above. Nevertheless, the take-home message of my dissertation is that the assessment of individual differences in personality is important for an improved understanding of basic brain functions and the impact of their dysfunction on behavior. This is particularly necessary to advance the understanding of mental disorders, moving beyond the grouping of individuals into categories. And this approach would hopefully reduce stigma attendant with mental illnesses.

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